THE BEHAVIOUR AND NEEDS OF INFANT MAMMALS

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AN infant has certain very obvious needs: he must be allowed to breathe, he must be fed, and he must be kept warm. His behaviour helps to ensure that these needs are satisfied. Attempts have indeed been made to describe all behaviour, and not only that of infants, in terms of homœostatic function. In an extreme form this point of view might be expressed in eleven words: all behaviour tends to maintain, or to restore, specific bodily states. It might be added that survival depends on the maintenance of these states. A corollary of this notion is that all learning depends on " reinforcement ": that is, that learning depends on getting something—such as food—that helps to keep the body in a steady state.

Probably nobody now holds these views in just these forms; but highly simplified propositions of this sort have their uses. The homœostatic concept has encouraged a matter-of-fact analysis of behaviour and of its physiological basis. Another notable generalisation has played an important part in the history of psychoanalysis: at one time Freud held that behaviour could be explained as a product of two " drives " (*Triebe*, sometimes translated as " instincts "). These were first, the erotic (a term given a very wide and sometimes ambiguous meaning in psychoanalysis), and secondly, the self-preserving.

The controversies that have raged around these notions are familiar, and I shall not discuss them in a general way. My concern is with the internal springs of behaviour (" motivation ") in infancy, and with some ways and consequences of altering them. One can be more precise about this subject now, because recent work on laboratory animals has brought new data and greater diversity to our picture of infant behaviour.

Behaviour as Homœostatic

First, something can be learnt from the items of infant behaviour which have an obvious homœostatic function. An infant's behaviour is in some respects like that of the adult stage of less complex animals: much of it is stereotyped and common to all other infants. (This is true, despite the equally important fact that from birth each infant has a distinctive personality of its own.) Bowlby (1958) has discussed the infant's stereotyped acts from the point of view of psychopathology. His list, with one addition is: sucking, head-turning, crying, smiling, clinging, and following. (Babbling, too, is universal, but falls into a separate category.)

Sucking serves an imperative need; typically it appears the moment it is called for, provided there is something to suck.

Head-turning (Prechtl 1958), which is associated with sucking, occurs " automatically " in the newborn infant when the skin near the mouth or of the lips is lightly touched. At first the movement is not directed, but soon the head turns towards the source of the stimulus. Clearly these responses enable the infant to find the nipple. There is a parallel in the work of Tinbergen and Kuenen (1939) on thrushes (*Turdus*): the newly-hatched birds at first respond to a suitable visual stimulus, such as that provided by a parent, by opening their mouths (gaping) and facing upwards, but later they gape towards the stimulus. This comparison serves to emphasise the stereotyped character of the response, and also the fact that it is not wholly rigid: even so simple an act changes with time, perhaps as a result of one of the several processes we call learning.

Crying is of several kinds, and much remains to be learnt about them. Of whatever kind, it is a social signal. In animal behaviour there are many examples of stereotyped acts, appearances, or odours which provoke equally stereotyped complementary responses. The gaping of young birds and the parents' response are examples, and there are many others in courtship ceremonies and territorial displays. The crying of infants is fairly stereotyped, and certainly tends to evoke a response from any adult present; but it is typical of our own species that the adult behaviour is *not* stereotyped. In other words the movements performed are much less predictable than they would be in other species, and reliable prediction requires knowledge of local customs or even of the person.

Social smiling is the indiscriminate but delightful greeting which appears in the early weeks and lasts for some months, until the child learns to recognise individual people. It can be evoked by any face, or even by a hideous mask. It is said that some mothers, faced with an unwanted child, quite change their attitude once smiling begins. Smiling is evidently a social signal with obvious survival value. Again, the responses it evokes are not stereotyped.

Clinging is perhaps more a relic of our primate ancestry than an important act now; but we shall see below that it is possible to underestimate the importance of bodily contact.

Finally there is *following*, which in our own species develops rather later than the other examples. It is exceedingly important in some species of mammals and birds; in the latter it has made possible the study of a process, called imprinting, which usually takes place only during an early and rather brief sensitive period, and which may establish the young animal's relationships with its own species (reviewed by Hinde 1960).

Many kinds of behaviour are developed more readily in early life than later—as in learning a language or teaching a dog tricks—and it is surprising that sensitive (or " critical ") periods have only now begun to be systematically studied. Today it is at least clear that the early months, weeks, or days of a mammal's postnatal life include a number of sensitive periods for the development of a variety of functions (reviewed by King 1958). They are usually not sharply bounded: the optimum phase is followed by a gradual decline in ability to develop the specific kind of behaviour.

" Drives "

The six patterns of infant behaviour listed above are not only stereotyped and found throughout our whole species: they are also substantially independent of each other. Granted, sucking, head-turning, and crying are all liable to be influenced by hunger; but all three can occur in the absence of hunger. Smiling, clinging, and following are quite separate. With one qualification to be noted later, there is no evidence that any single process or agency—whether we call it a drive or not—controls them all; nor that there are two such drives. The external stimuli which evoke the various acts are also different: crying is often a product of changes inside the body, but it may be provoked by a loud noise or by cold or other skin discomfort; head-turning is usually a response to a tactile stimulus; smiling depends on visual stimuli; and so on.

This picture of independent patterns of behaviour, set going in different ways, is as a first approximation in accord with current views of animal behaviour (e.g., Hinde 1959). This becomes clearer if we look at the behaviour in evolutionary terms. Each stereotyped action, like a structure or any other feature, has survival value; but natural selection can bring about the ability to perform it by any of a variety of physiological mechanisms. The physiology of each act has therefore to be studied separately if we are to understand it.

A familiar feature of many stereotyped acts is that they are more readily evoked the longer the interval since they were last performed. This is related to the homœostatic function of activities such as breathing and eating, but the " build-up of drive " is also seen in sexual behaviour. This relatively short-term build-up effect is a general feature of behaviour at all ages. Another consequence of deprivation, however, is more relevant to the special needs of infancy. As an example we may ask what happens when an infant is deprived for long of the opportunity to suck, or at least to suck with the usual intensity. This can, of course, happen without shortage of food, as in some bottle-fed babies.

Ross et al. (1957) have reviewed this subject. The evidence is conflicting, but there is little doubt that in puppies at least early deprivation leads to an increased tendency to suck later, even though nutrition is adequate. But undernutrition in early life too can lead to excessive sucking. To minimise the tendency to suck (smoke? or chew gum?) in later life, it seems that both plenty of sucking exercise *and* a good diet are needed. This does not fit an interpretation in terms of two drives, nor with the notion that infant behaviour is directly and exclusively homœostatic. Sucking is to some extent performed without regard to hunger (as one can readily infer from observing an infant); subjectively a baby (or other young mammal) likes sucking for its own sake. To call this behaviour erotic is to extend the meaning of " erotic " to " enjoyable ". We may suppose that natural selection has ensured that babies will suck vigorously; and that this is due in part to a neural mechanism for sucking which operates on its own. The same must apply to other stereotyped behaviour, such as smiling, though there is no evidence that being deprived of the opportunity to smile has effects analogous to those of not enough sucking. If one wished to persist in speaking of drives, one would have to assume the existence of a number of separate drives (and just this is indeed done in some psychological writings).

A further conclusion may be drawn if we accept that sucking too little in infancy is followed by too much later. This is that deprivation in early life can have a significant effect on adult behaviour *even when no obvious disturbance of homœostasis is involved.* It is as if the young mammal has to learn to inhibit behaviour such as sucking, and cannot do so if it does not perform the behaviour at the usual intensity. Evidently an early sensitive period provides the only, or the main, opportunity for the inhibition to arise.

Cutaneous Stimulation

So far the discussion has been on the performance of specific *activities*. These are of course always accompanied by a sensory (especially proprioceptive) feedback. But now we may turn to external stimulation, and in the first place to a particular kind—cutaneous stimulation—notably that provided by the mother.

Mammals are in general contact animals; they huddle together. In some, including rats (*Rattus*) and baboons (*Papio*), amicable behaviour is signalled by specific forms of contact; and of course coitus is preceded by it. (There are obvious human analogies; but the ways in which we " signal " an amicable attitude are culturally determined, not stereotyped for the whole species.) The first specific cutaneous stimulation experienced by a newborn mammal is often from its mother's tongue; this licking is, at least in rats and mice, essential for establishment of the reflexes of elimination (Reyniers and Ervin 1946).

Cutaneous stimulation in early life has, however, more complex and subtle effects than merely initiating reflexes. Much work has been done to show the effects of stroking the skin on the subsequent development of young laboratory rats. The stimulation usually takes the form of a fixed daily amount of stroking or " gentling " by the experimenter; a finger or a brush may be used. Control rats are usually not handled at all.

Growth has been studied by Weininger et al. (1954, 1956), McLelland (1956), and Levine and Otis (1958), among others. Their observations conflict in some details, but agree on the essential that the stimulated rats grow more quickly. This does not entail a greater consumption of food, but is evidently due to more efficient food utilisation. Levine (1960) suggests that stimulation induces a higher rate of development generally: for instance the cholesterol content of the brain, and hair growth, are both increased in stimulated animals. However, growth-rates in themselves are not necessarily important unless one is breeding for the table. But the effect on growth is accompanied by an improvement in intelligence. Levine (1956) used a conditional avoidance as a criterion of learning ability, and found that handled rats learned it more quickly. The handling was more effective before the age of 20 days than at 50–70 days—a typical example of a sensitive period.

Still more important are studies of resistance to various sorts of *stress* (reviewed by Bovard 1958, and Levine 1960). Some of this work has been done on mice. The earliest work was on the effects of parathyroidectomy, published nearly 40 years ago and long neglected. Hammett (1921, 1922) found that one group of rats survived the operation for much longer than another; and the only significant difference between them was that the resistant rats had been regularly handled by laboratory attendants. When the subject was taken up systematically, during the 1950s, various adverse conditions were used to test the effects of handling: they included immobilisation (by binding animals up), prolonged deprivation of food and water, and exposure to cold. Always the handled animals withstood the stress better than the controls. A correlate of these observations is that handling reduces " emotionality ": a handled animal, on being placed in an unfamiliar open space, explores confidently and shows little sign of exceptional autonomic activation, whereas a non-handled control tends to freeze and to defæcate and urinate excessively.

At first some emphasis was laid, at least by implication, on the need to stroke the stimulated animals, but recently the emphasis has been put more on the mere fact of handling: indeed, resistance to stress can be induced merely by picking up very young rats, putting them in a box, and then replacing them in their cage. It now seems possible that general stimulation of the animals is important, and that the implications of the word gentling are inappropriate.

A Physiological Basis

It has in fact been suggested that handling in infancy constitutes a mild " stressor " (e.g., Denenberg and Karas 1959): that is, it activates the pituitary-adrenal system which, in the adult, plays a major part in the adaptive response to cold, injury, poisoning, infection, and so on. It is as if the ability to respond effectively to stress in later life has been brought to a higher level by the mild early stimulation. One index of the response to stressors is the output of corticotrophin by the pituitary, and the consequent secretion of steroids by the adrenal cortex. If handled animals are compared with controls in the absence of stress, the steroid output is the same in both groups. If both groups are then subjected to stress, say, by a painful stimulus or a toxin, steroid output rises in both but is higher in the non-handled animals: this evidently reflects their greater susceptibility to the ill effects of the stressor. But if steroid output is recorded during the first 15 minutes after a severely noxious stimulus, such as electric shock, the handled animals are found to have the higher output. Evidently it is the delay in making the endocrine response that is maladaptive (Levine 1960).

An analogous speeding up is found in development: rats handled in the first few days of life produce an effective response (corticotrophin secretion) to stressors at 12 days, whereas non-handled rats do not do so until 16 days. Here is an obvious resemblance to the more prosaic effects of early experience: for instance, mice reared from birth in a cold environment resist cold at 3 weeks better than mice reared in a warm environment (Barnett et al. 1960).

It seems that a mammal deprived in early life of certain forms of stimulation (not yet fully identified) is enfeebled. In a sense, an infant mammal *needs* this kind of stimulation, even though it is not essential for survival in the way that, say, food is essential.

Stimulation from Exploring

The importance of stimulation in early life is equally clear from studies of the effects of exploratory behaviour, reviewed more fully elsewhere (Barnett 1958). This behaviour consists typically of wide-ranging movements in which a recently visited place is less likely to be entered than an unfamiliar one. It is performed independently of primary needs such as hunger. Indeed in some circumstances such needs may interfere with it; but the impulse to explore, to seek a variety of stimulation, and to experience novel conditions is very powerful. Rigorous studies have been mainly on rats (though also on cockroaches [*Blattella*], monkeys [*Macacca*], and chimpanzees [*Pan*]). Rats sometimes seem to behave as though they were easily bored and so were obliged continually to seek new experiences. Obviously this applies even more to our own species. (Bertrand Russell once remarked that intelligent children spend much of their time in a state of boredom.)

The facts about exploratory behaviour, and the tendency to seek novelty, have many theoretical implications. They do not fit into any simple interpretation of behaviour in terms of homœostatic drives: in subjective terms, exploration and variety of experience are enjoyed in themselves, without regard to consequent rewards such as finding food, a mate, or shelter. It follows that the so-called Nirvana principle, according to which behaviour is directed towards reducing stimulation to a minimum, is wrong. The Freudian notion that the drives are wholly directed by a need or desire to nullify the effects of disturbance, internal or external, is mistaken.

It may be asked, if exploratory behaviour is independent of primary need, what, in an animal such as a rat, is its function? Part of the answer is that this behaviour does, in the long run, help the animal to satisfy its needs for food and so on: during exploration the animal learns incidentally about the amenities and resources of its environment, and later makes use of this knowledge when need arises. But, especially in early life, exploratory behaviour and the consequent diversity of experience have an additional importance. I mentioned above that cutaneous stimulation can improve the intelligence, or learning ability, of rats. It seems possible that this is a special case of a well-established general phenomenon: rats and other mammals are much influenced in their adult learning ability by diversity of stimulation in the first few weeks of life. Rats brought up in a spacious enclosure containing a variety of objects can learn to find their way through mazes more readily than controls reared in the usual confined quarters. This sort of observation supports Hebb's (1949) important distinction between early and late learning in mammals. Learning in infancy, so obviously slow and inefficient, is somehow organising the great mass of connecting neurons in the forebrain so that, later on, rapid responses and rapid learning can take place. In the early stages the principal process is learning to learn.

There is much to be discovered about just how general this " deutero-learning " is. How far does it generalise from one sensory modality to another? Forgus (1955) reared one group of rats in a large and complex environment in which they had much visual and motor experience, and another group in which visual stimulation was the same but the opportunity to move around was much less. The second group learned mazes better in the light; but the first group was better in the dark, when evidently learning had to be based on kinæsthesia.

The importance of variety of experience in the development of intelligence must make us reflect on the desirability of confining young children for long periods to prams; in general it should make us think further about the best environment for mother and child if plenty of freedom of movement is needed for full development of all the faculties. Other data too suggest comparisons with our own species. Cooper and Zubek (1958) studied two kinds of rats, one selected over many generations for " maze-brightness " (or intelligence in dealing with a certain kind of problem), and the other selected for " maze-dullness ". Rats from these two strains were tested by rearing them in different conditions, and then they were examined for learning ability. The bright rats were not made more intelligent by rearing in an enriched environment; but dull rats were improved by this more stimulating upbringing and they reached the level of the bright rats. Similarly, dull rats reared in exceptionally restricted environments were not made more stupid; but bright rats so reared were made to resemble dull rats. To what extent, one wonders, does this sort of thing happen under different kinds of schooling?

" Mothering "

The study of the effects of stimulation in early life has, then, thrown a few gleams of light on two ill-explored areas. The effects of skin stimulation tell us something about the development of the emotions, and of resistance to unfavourable conditions; while exploratory behaviour, or, more generally, variety of stimulation, influences the growth of intelligence.

Work by Harlow and his colleagues has now further extended our ideas on the importance of stimulation in infancy (Harlow and Zimmerman 1959). It has been known for some time that young goats (*Capra*) display excessive signs of disturbance (anxiety) in stressful situations if they are not with their mothers (Liddell 1956). There is even evidence of the same sort of thing in rats (Lubow and Marcuse 1956). Harlow has pursued this line of inquiry with monkeys (*Macacca mulatta*). He has shown that an infant monkey behaves atypically if deprived of the presence of a mother: instead of exploring its surroundings confidently, or sleeping peacefully, it huddles in a corner, rocks backwards and forwards, and displays other signs of anxiety and distress. This behaviour can be prevented by giving the monkey a substitute mother to cling to. The models used are roughly the size and shape of an adult monkey; to be fully effective they also have to be of the right texture, and to stand vertically. The young creature clings to the model, sleeps on it, climbs over it, and rubs itself against it; it uses it as a base from which to explore the world around it, and confidently to investigate strange objects made available by the experimenter. The model is also a refuge to resort to when frightened.

Clearly, cutaneous stimulation plays an important part in this situation, but it is still uncertain how this is related to the effects of handling described above. Harlow's observations seem more obviously comparable to those of Bowlby (e.g., 1958, 1960) on the effects of maternal deprivation in early life, and especially to the resemblance of the deprived child's response to that of an adult mourning the death of a loved one. One of Bowlby's most important theses is that a child must be attached to a single mother-figure if severe disturbance of behaviour is to be avoided. Much has now been written about this notion, starting with studies of the ill effects on young children of staying long in hospitals or other institutions (e.g., Bakwin 1942). Both lines of study, on animals in laboratories and on children in institutions, have obliged us to think again about " motivation " and " needs ". Harlow and Zimmerman (1959), for instance, remark that the attachment of a young monkey to an inanimate substitute mother cannot be based on " drive reduction ", as that term is ordinarily understood, since the monkeys resorted to the models whether they were fed on them or not. Indeed, they preferred to cuddle comfortable mothers, on which they were not fed, rather than to cling to uncomfortable ones on which they could feed. Here then, once again, is a need for a kind of stimulation which is not essential for survival. This may seem obvious enough to some; but it is useful to have the point made unequivocally, on the basis of experiment.

Bowlby (1958, 1960), for his part, is trying to combine the understanding derived from psychoanalysis with conclusions from laboratory experiments. One of his most important proposals is that the primary cause of anxiety is early separation from the mother, and not a consequence of sexual motivation, in any sense of that term. The experiments on young monkeys, and the physiological analysis of the effects of stimuli in early life, together suggest a way in which these questions can be studied rigorously.

The Analysis of Drive

The new growth in behaviour studies is in fact a product of the detailed analysis of individual problems. Students of behaviour select particular phenomena, such as the apparently undirected movements of young mammals, or unexpected death under stress, and try to define the exact conditions in which they arise; sometimes they can relate behaviour to internal processes such as the secretion of hormones or activation of hypothalamic nuclei.

This method does not at present promise any grand synthesis, such as Freud's theory of human motivation. On the contrary, the tendency is to qualify the simple generalisations which have provided a framework for much writing and research during the past decades. This is evident if we look again at the Freudian drives. The conditions in which the standard acts of infancy are evoked give no support to unitary or binary theories of drive.

However, it does not follow that we must abandon all notions of relationships between different kinds of behaviour.

First is the question of " general drive state ". This refers to the internal processes which determine the level or intensity, rather than the nature, of an individual's activity. Hebb (1955) has equated it with the level of arousal, decided by the degree of activation of the reticular formation of the brain-stem. Whether this is justified or not, little seems to be known either of general drive or of arousal in infancy. Yet, if we are to assess theories of drive in early life, we need to know how far it is legitimate to talk of general drive, and in precisely what sense.

Second is the question of substitutive behaviour (cf. Barnett 1955). In animal behaviour one activity is sometimes substituted for another: a male wild rat may fight another male after being rejected by a female, when otherwise he would not have done so. It is also sometimes found that, when two activities, such as attack and flight, are simultaneously aroused, a third one is performed. Further, when an object towards which an activity is directed is removed, another object may be substituted (the redirection of zoologists; displacement in psychoanalysis). What connection this sort of thing has with general drive or with arousal is still unresolved.

Perhaps, however, the interaction between different kinds of behaviour, or between the processes which control them, has an application to psychoanalytic theory. In biology, as in ordinary speech, " sexual motivation " refers to the internal springs of sexual behaviour, that is, of courtship, coitus, and allied acts. If such behaviour is prevented, some alternative may be substituted. The alternative behaviour, ordinarily connected with, say, the quite separate function of ingestion, would then, in psychoanalytic usage, be called erotic. It seems that the Freudian unitary or binary theory of drives is an unjustified extension of the important observation that one kind of motivation can influence the performance of acts usually associated with another kind. On these lines a theory of the springs of behaviour in infancy might, perhaps, be developed—a theory in which the conclusions of psychoanalysis are married to those derived from experiment.

Conclusions and Summary

By " needs " it is convenient to refer to requirements for optimum performance, and not merely to what is a sine-qua-non for survival. Granted, to identify the optimum is not always easy; but agencies which improve " intelligence " may be included, and so may conditions which increase resistance to a stressor such as infection. There are also social needs: a young mammal requires certain experiences which enable it later to fit its behaviour to that of other members of its species. Both intelligence and social behaviour are influenced in major ways during early sensitive periods of development.

Intelligence, resistance to stressors, and social behaviour are all influenced by various sorts of stimulation in early life:

1. The stimulation derived from variety of experience, resulting from investigation, manipulation, and play, promotes a kind of learning—the kind that makes possible a rapid acquirement of useful habits and particular skills in later life.

2. The stimulation which a laboratory animal receives from being handled increases its ability to cope with noxious agents later.

3. The stimulation that a baby monkey gets from a model mother (or an infant from his attachment to a particular person) is more enigmatic; but it probably helps in the development of both intelligence and social behaviour.

Clearly it is to the biological advantage of a young mammal to be stimulated in these ways: that is, it has survival value. We must therefore expect that the behaviour of young mammals will bring them into conditions in which they will receive stimulation. In other words they will display a "drive" (for instance) to explore; and this is indeed found in the sense that they (and adults too) explore in the absence of specific need—for example for food, and even at the expense of satisfying hunger. Hence we find not only a propensity for acts which satisfy homœostatic needs but also other activities strenuously pursued.

That there are independent impulsions for a number of kinds of behaviour is shown when we study the stereotyped actions of infancy, such as sucking and smiling. These are not, or at least not wholly, dependent on states of deprivation, such as hunger, but are often performed independently; they are influenced also by different external stimuli. There is no basis here for a unitary theory of drive.

This does not mean that there is no interaction between different activities or their internal determinants. Interaction is evident in substitutive behaviour, such as, perhaps, functionless sucking. A particular kind of behaviour can be stimulated, and at the same time prevented by the removal of the object to which it is directed or by the simultaneous activation of another kind of behaviour. In either case an alternative act may be performed. This sort of thing, clearly evident in the displacement behaviour studied by zoologists, is perhaps also the basis for the Freudian notion that so much of human behaviour is erotically motivated.

REFERENCES

Bakwin, H. (1942) *Amer. J. Dis. Child.* **63**, 30.
Barnett, S. A. (1955) *Lancet*, ii, 1203.
— (1958) *Brit. J. Psychol.* **49**, 289.
— Coleman, E. M., Manly, B. M. (1960) *Quart. J. exp. Physiol.* **45**, 40.
Bovard, E. W. (1958) *Psychol. Rev.* **65**, 257.
Bowlby, J. (1958) *Int. J. Psycho-Anal.* **39**, 350.
— (1960) *ibid.* **41**, 1.
Cooper, R. M., Zubeck, J. P. (1958) *Canad. J. Psychol.* **12**, 159.
Denenberg, V. H., Karas, G. G. (1959) *Science*, **130**, 629.
Forgus, R. H. (1955) *J. comp. physiol. Psychol.* **48**, 215.
Hammett, F. S. (1921) *Amer. J. Physiol.* **56**, 196.
— (1922) *Endocrinology*, **6**, 221.
Harlow, H. F., Zimmermann, R. R. (1959) *Science*, **21**, 421.
Hebb, D. O. (1949) The Organization of Behavior. New York.
— (1955) *Psychol. Rev.* **62**, 243.
Hinde, R. A. (1959) *Anim. Behav.* **7**, 130.
— (1960) *In* Current Problems in Animal Behaviour (edited by W. H. Thorpe and O. L. Zangwill). London.
King, J. A. (1958) *Psychol. Bull.* **55**, 46.
Levine, S. (1956) *J. Personal.* **25**, 70.
— (1960) *Sci. Amer.* **202**, 81.
— Otis, L. S. (1958) *Canad. J. Psychol.* **12**, 103.
Liddell, H. S. (1956) Emotional Hazards in Animals and Man. Springfield, Ill.
Lubow, R. E., Marcuse, F. L. (1956) *J. comp. physiol. Psychol.* **49**, 462.
McLelland, W. J. (1956) *Canad. J. Psychol.* **10**, 19.
Prechtl, H. F. R. (1958) *Behaviour*, **13**, 212.
Reyniers, J. A., Ervin, R. F. (1946) *Lobund Rep.* **1**, 1.
Ross, S., Fisher, A. E., King, D. (1957) *J. genet. Psychol.* **91**, 63.
Tinbergen, N., Kuenen, D. J. (1939) *Z. Tierpsychol.* **3**, 37.
Weininger, O. (1956) *J. comp. physiol. Psychol.* **49**, 1.
— McClelland, W. J., Arima, R. K. (1954) *Canad. J. Psychol.* **8**, 147.

THE NATURE OF VAGINAL DISCHARGE

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MANY specimens of vaginal discharge are sent to this laboratory with a request for "organisms and sensitivities". The assumption seems to be that the discharges are due to bacterial infection, and the object of this study was to decide how often this is true. It is based upon 595 specimens received either from the family doctor or the outpatient department. In every case the patient's complaint (among others) was of a discharge which was excessive in amount, irritating, or offensive. Most of the patients were in the reproductive period of life (here reckoned arbitrarily as 15–50), and those outside these limits have been considered separately. As far as has been possible no woman has been included who had had a baby or a gynæcological operation within the previous three months. No attempt has been made to distinguish effects which might be due to repeated childbirth, cervical erosion, or prolapse, nor has any account been taken of the stage in the reproductive cycle at which the specimen was taken.

In addition to the 595 specimens from patients with a discharge, 65 specimens of normal vaginal secretion were examined. These were obtained from a Family Planning clinic from women with no complaints and no obvious evidence of abnormality.

Material and Methods

All the specimens were received on cotton-wool swabs. The majority were examined within a few hours of being taken. The material was first examined as an emulsion in normal saline and as a gram-stained film. The former is as good a way as any of revealing the presence of *Trichomonas vaginalis*, and at the same time allows a reasonable estimate of the relative numbers of epithelial cells and leucocytes (Magath 1938). Because the discharge is not always homogeneous the stained film is less satisfactory for observing the cytological appearances, but it shows the yeast-like fungi and the number and kinds of bacteria. Experience showed that a distinction must be made between a few scattered yeast-like fungi and an abundance of such cells accompanied by mycelial elements (Liston and Cruickshank 1940). Since a few *Candida* spp. are not uncommon in the normal vaginal introitus, only those specimens with many yeast-like fungi together with mycelium were recorded as "positive". Because they have no quantitative value, mycological cultures were abandoned after a trial. Bacterial cultures were made on horse-blood agar, aerobically and anaerobically. These gave only a partial, and sometimes misleading, picture of the vaginal flora: some genera—e.g., lactobacilli *—grow poorly or not at all on this medium, while coliform bacilli tend to overgrow all others. In practice, a subjective appraisal of the bacterial flora was made on the combined results of direct examinations and cultures. The reaction was estimated by B.D.H. "narrow range" indicator papers; these gave consistent results and seemed to be accurate enough for the purpose.

Composition of Vaginal Discharge

The normal vaginal secretions consist of: (1) exfoliated epithelium; (2) scanty transudated leucocytes, (3) cervical secretions, and (4) bacteria.

The main interest of this study was bacterial infection, and because, in almost every site and circumstance, the reaction of the body to local infection is the production of pus, it seemed reasonable to make the presence of abnormal numbers of leucocytes the basis of a tentative

* Throughout this paper "lactobacillus" is preferred to the ill-defined "Döderlein's bacillus".

TABLE I—VAGINAL DISCHARGE (AGED 15–50)

Group	No.	Leucocytes	Lactobacilli	pH
Patients with discharge ..	405	0/±	+	4·3–5·5
	13	+	+/±	4·9–5·8
	143	++	0	5·2–7·3
Total	*561*	..	..	
Normals	65	0/±	+	4·3–5·2

classification of vaginal discharges. In practice, it is not difficult to decide whether the number of leucocytes exceeds the normal. A frankly purulent discharge is obvious microscopically, and most of those seen were of this nature. An upper arbitrary limit of normality had to be established: a discharge has been classified as purulent in this series if the number of leucocytes in a microscope field (× 500) exceeded 25, or was more than the number of epithelial cells. It was expected that the "showers of leucocytes" seen immediately after ovulation might invalidate this rough classification, but this did not happen.

Table I shows the results of this classification applied to discharges from 561 women of reproductive age and to the vaginal secretions of 65 apparently healthy women. It will be seen that the presence of pus is associated fairly consistently with two other characters. Such discharges are, on the whole, less acid than the discharges with few or no leucocytes, and they rarely contain lactobacilli. There were, however, 13 patients whose discharges contained more pus than could be considered normal, but which at the same time contained numerous lactobacilli but no protozoa, yeast-like fungi, or evidence of specific bacterial infection. It may be significant that 8 of these were in the later months of pregnancy and 1 had a large prolapse.

Table II shows a more detailed analysis of the 418 discharges which contained little or no pus. Four-fifths of them seemed indistinguishable from the 65 normals in reaction, cytological appearance, and flora. The other fifth contained large numbers of yeast-like fungi and

TABLE II—VAGINAL DISCHARGE WITHOUT LEUCOCYTES (AGES 15–50)

No. of specimens	Lactobacilli	*T. vaginalis*	*Candida* spp.	Bacteria	pH
354	+	0	0	N.S.P.	4·3–5·8
64	+	0	++	N.S.P.	4·3–5·2
Total *418*	..	..	..	..	..

N.S.P. = no specific infection.

mycelia; but in these, too, the cells and bacteria differed in no obvious way from those of the group as a whole. The bacterial flora ranged from lactobacilli alone to a mixture of lactobacilli with micrococci, diphtheroid bacilli, vibrios, and coliform bacilli. No organism or group of organisms (except lactobacilli) were found to be associated habitually with any other element in the discharges nor were any of the bacteria commonly pyogenic in man ever found. In general, the flora consisting of lactobacilli alone was commonest in the younger women. With increasing age and repeated childbirth the proportion of other organisms increased and the pH tended to rise. At about the menopause the reaction became still less acid, but the changes at this time take place gradually and anomalous findings were not uncommon—e.g., lactobacilli occasionally persisted into old age.

The purulent discharges showed quite a different picture (table III). Over 90% of these contained *Trichomonas vaginalis*. The bacterial flora accompanying this protozoon might be profuse or scanty, but always appeared to consist of the same species as were found in the discharges without pus. Lactobacilli were, however, seldom present. *Candida albicans* was found only once in association with *T. vaginalis*.

In only 9 patients of reproductive age did it seem probable that bacterial infection was the cause of a purulent discharge. The discharges had the following characteristics: (1) abundant pus; (2) *T. vaginalis* absent; (3) pH about neutrality, whereas in those showing *T. vaginalis* it ranged from pH 5·2 to 6·4; and (4) an organism known to be pyogenic in other sites and found here in pure or almost pure culture.

The organisms found in these 9 discharges are rarely if ever found in the healthy vagina but are not uncommon after childbirth. They were *Streptococcus pyogenes* (groups A and C) (5), *Staphylococcus aureus* (3), and *Escherichia coli* (1). The last was an infected chemical vaginitis. *Neisseria gonorrhœæ* was not found among adults in this series.

TABLE III—PURULENT VAGINAL DISCHARGE (AGES 15–50)

No. of specimens	Lactobacilli	*T. vaginalis*	*Candida* spp.	Bacteria	pH
134	0	+	0	N.S.P.	5·2–6·4
9	0	0	0	P.C.	6·1–7·3
Total *143*	..	..	..	..	..

P.C. = pure or almost pure culture.

Discharge in Children and Older Women

Vaginal discharges in patients outside the age-group 15–50 seemed to differ considerably from those just described, but they were so few that it would be unwise to draw any firm conclusion from them (table IV). Judged by the same criteria 13/15 discharges in children were due to bacterial infection. 2 were gonococcal, 7 were due to *Str. pyogenes* (groups A, C, and G), 2 to *Staph. aureus*, and 2 to coliform bacilli. 2, at least, were associated with foreign bodies. In older women 15/18 discharges were attributed to bacterial infection. 1 was due to *Str. pyogenes* (group A), 3 to *Str. fæcalis*, 1 to *Staph. aureus*, and the remainder to coliform bacilli. The group included women with senile pyometra and with carcinoma of the cervix.

A Tentative Classification for the Laboratory

In women of reproductive age there seem to be four main types of vaginal discharge, which may be divided into two groups: (1) those discharges containing little or no pus (group I), and (2) those containing abundant leucocytes (group II).

Group Ia

A discharge consisting largely of epithelial cells, and lactobacilli, alone or mixed with commensal organisms, but containing no yeast-like fungi or protozoa: pH 4·3–5·8.

Cruickshank and Sharman (1934) suggested that the non-purulent discharge of virgins was no more than an exaggeration of the normal vaginal secretions brought about by some endocrine mechanism. Since, throughout the reproductive period, this type of discharge does not differ qualitatively in any way from the secretions of the healthy vagina, it seems reasonable to extend this dictum

TABLE IV—VAGINAL DISCHARGE (CHILDREN AND ELDERLY WOMEN)

No. of specimens	Ages (yr.)	Leucocytes	*T. vaginalis*	*Candida* spp.	Bacteria
13	0–14	++	0	0	P.C.
3		0	0	0/±	N.S.P.
Total *16*	..	..	..	..	..
15	51+	++	0	0	P.C.
3		0/±	0	0	N.S.P.
Total *18*	..	..	..	..	..

up to the time of the menopause. The cause of this excessive secretion is obscure: some sufferers benefit by cautious treatment with œstrogens (Russell 1960).

Pregnancy may exaggerate the secretion. After childbirth the discharge may become purulent for days or weeks but this change is not permanent. With increasing age there is usually a change in the flora from lactobacilli alone to a mixed flora in which the lactobacilli themselves may be scanty towards the menopause. In parallel with these changes, the reaction tends to become less acid. The process may be attributed to a variety of causes—mechanical, endocrine, and biochemical—which are to some extent interrelated. In the individual patient, the low pH together with the absence of pus, fungi, and protozoa suggest strongly that the discharge is not due to any extraneous agent.

Group Ib

A discharge similar in all respects to Ia, but with large numbers of yeast-like fungi and much mycelium.

" Monilial vaginitis " is beyond doubt a clinical entity, commonest in pregnancy and characterised by severe irritation (Jeffcoate 1955). The name, however, may be a misnomer.

Yeast-like fungi of several kinds are not uncommon in the vagina but, according to Feo and Dellette (1953), *C. albicans* is the species usually found in patients with the typical clinical history. 15 strains of such fungi from this series were examined systematically and all were of this species.

Adair and Hesseltine (1936) state that many leucocytes are present in the discharges associated with *C. albicans*. In this series any evidence of purulent inflammation has been conspicuously absent from these discharges. In other sites where *C. albicans* grows readily—e.g., the mouth and the skin of the buttocks in infants—the fungus forms a thick mat of mycelium and exudate which contains few leucocytes and which peels readily from the underlying surface. In even the most severe infections the inflammatory process appears to be *on* rather than *in* the epithelial surface. McCrea and Osborne (1960) have described the histological features of a fatal infection of the œsophagus in piglets due to this fungus. Their sections show a matted felt of mycelium containing scanty leucocytes. The underlying mucous membrane is œdematous, but the connection between this and the mycelial felt is limited to a few hyphæ which appear to penetrate the superficial layers of cells without causing an inflammatory reaction.

There are some other observations which would seem to distinguish parasitism by *C. albicans* from a simple inflammation of the vaginal wall. Karnaby (1954) found it difficult to induce experimental infection in the healthy vagina. Natural infections, on the other hand, are, according to most authorities, often resistant to treatment and liable to frequent relapse. Successful treatment of the candidal infection (e.g., with nystatin) may be followed by a profuse non-purulent discharge from which *C. albicans* cannot be isolated.

In vitro the optimum reaction for the growth of *C. albicans* is between pH 4·4 and 5·2. The fungus grows readily in normal vaginal secretion (diluted 1/5 with physiological saline) at pH 5·0 without any added source of carbohydrate. Rogosa and Sharpe (1960) have suggested that the vaginal lactobacilli obtain carbohydrates directly or indirectly from the glycogen in the desquamated epithelium. *C. albicans* may possibly draw on the same source. As suggested by Davis and Pearl (1938) the prevalence of candidal infections in pregnancy may be due to the excess of glycogen in the epithelial cells at that time. If this is so, parasitism by *C. albicans* should not be described as an infection of the vagina but of the vaginal secretions. Probably, it is commonly an infection of a secretion which is already excessive (as described in group Ia). This suggestion may be equally applicable to other sites favoured by this fungus.

Group IIa

A purulent discharge containing *T. vaginalis* and a mixed and various bacterial flora. Lactobacilli and yeast-like fungi rarely found: pH 5·2–6·4.

Trichomonal infestation is a clinical entity, the confirmation of which does not present any great difficulty in the laboratory provided that the material is fresh.

" Trichomonal vaginitis " has been said to be a specific streptococcal infection with a superadded protozoal infestation (Hesseltine 1933). In this series there was no evidence for this view. Indeed, the most striking thing about the associated bacterial flora was its variety. As was shown by Kessel and Gafford (1940) the bacteria found in trichomonal discharges are, except for lactobacilli, the same as those found in the normal vagina.

Group IIb

A purulent discharge with a reaction about neutrality; *T. vaginalis*, lactobacilli, and yeast-like fungi absent; but a pyogenic organism present in large numbers and often in almost pure culture.

These discharges are rare in women of reproductive age but are not usually difficult to recognise. Some at any rate are a sequel to damage to the genital tract from some other cause. In children and elderly women, on the other hand, bacterial infection is the usual cause of vaginal discharge.

The categories suggested are mutually exclusive, but at either end of the reproductive era they do not cover every permutation of the several factors which may cause or modify the nature of vaginal discharge.

Gonorrhœal Infection

No material from a venereal diseases clinic was included in this series. No evidence of gonorrhœa was found in any adult patient, and for this reason it has been impossible to include gonococcal discharges in this classification. The kinds of discharge which have been noticed tend to be persistent afflictions, whereas even without treatment gonorrhœa in the adult is an acute and transient disease. Gonoccocal infections of the vagina in children do not differ obviously from any other pyogenic infections.

Frequency of the Causes of Vaginal Discharge

The literature on this subject is confused, either because investigators have drawn their material from a selected group (e.g., a venereal-diseases clinic) or because they have had an especial interest in one or other of the parasites thought to cause vaginal discharge. The proportion of patients harbouring *T. vaginalis* in this series (24%) is much the same as that found by many others. 12% were attributed to *C. albicans*, which is less than the figure usually given. This difference may be due to limiting the diagnosis to those patients whose discharges showed evidence of active fungal multiplication. The most obvious divergence of this series from others is in the large number of women (62%) with a discharge which differed in no obvious way (except quantity) from the normal vaginal secretions and which could not be

attributed to any extraneous cause. Many of these discharges (but by no means all) were sent by family doctors, and it may well be that patients with these " simple " discharges come to hospitals less often than those with more severe symptoms. It may be, too, that the growing interest in personal health leads women to complain to their doctors of symptoms which in an earlier age were borne in silence.

Summary

Of 561 specimens of vaginal discharge from women of reproductive age, 9 appeared to be due to bacterial infection. 134 were associated with *Trichomonas vaginalis*, and 64 with *Candida albicans*. The remainder were indistinguishable from normal vaginal secretion in any character except quantity.

13/16 vaginal discharges in children and 15/18 in women over 50 appeared to be due to bacterial infection.

A tentative classification of vaginal discharges based upon the reaction of the host and the parasite is suggested.

It is possible that *C. albicans* is parasitic, not on the vaginal wall, but on the secretions of the vagina.

My thanks are due to Mr. P. M. G. Russell for many interesting conversations on this subject and to Dr. Stella Henderson for supplying material from the Family Planning Clinic.

REFERENCES

Adair, F. L., Hesseltine, H. C. (1936) *Amer. J. Obstet. Gynec.* **32**, 1.
Cruickshank, R., Sharman, A. (1934) *J. Obstet. Gynæc. Brit. Emp.* **41**, 190, 369.
Davis, M. E., Pearl, S. A. (1938) *Amer. J. Obstet. Gynec.* **35**, 77.
Feo, L. G., Dellette, B. R. (1953) *ibid.* **65**, 131.
Hesseltine, H. C. (1933) *ibid.* **26**, 46.
Jeffcoate, T. N. A. (1955) *Med. World*, **82**, 136.
Karnaby, K. J. (1954) *Amer. J. Surg.* **87**, 188.
Kessel, J. E., Gafford, J. A. (1940) *Amer. J. Obstet. Gynec.* **39**, 1005.
Liston, W. G., Cruickshank, L. G. (1940) *Edinb. med. J.* **47**, 369.
McCrea, M. R., Osborne, A. D. (1960) *J. comp. Path.* **67**, 342.
Magath, T. B. (1938) *Amer. J. Obstet. Gynec.* **35**, 694.
Rogosa, M., Sharpe, M. E. (1960) *J. gen. Microbiol.* **23**, 197.
Russell, P. M. G. (1960) Personal communication.

ENDOSCOPIC EXAMINATION OF THE STOMACH AND DUODENAL CAP WITH THE FIBERSCOPE

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With illustrations on plate

SINCE a previous report on the fiberscope (Hirschowitz, Curtiss, and Peters 1958), work has progressed to the point where a clinically useful model of this completely flexible instrument has been made and used in the examination of the upper gastrointestinal tract. The current experimental model has been used successfully to examine the lower œsophagus, stomach, pyloric canal, duodenal bulb, and both afferent and efferent loops of jejunum for a distance of up to 12 in. beyond gastrojejunal anastomoses, all with sufficient resolution to describe fine mucosal detail. Furthermore, both still and movie photographs in colour have been taken through the instrument of the stomach and duodenum without additional illumination. Among the interesting findings are the observations on duodenal ulcer in situ and of a distinct sphincter at the apex of the duodenal bulb.

The Instrument

The fiberscope superficially resembles a conventional gastroscope, comprising a head which contains a lamp bulb, a prism, and a compound lens which focuses the image on to the distal (objective) end of the fibre bundle. The view is at right angles to the instrument. The shaft of the instrument contains the glass fibre bundle which transmits the image to the eyepiece and is *completely flexible throughout its entire length* (fig. 1).

The bundle is protected by a flexible flat bronze spiral which is also used to transmit torque. It is in turn covered by a smooth plastic sheath. The ocular (proximal) end contains a simple lens for magnifying the image from the proximal end of the fibre bundle, a ratchet for focusing the distal lens, and connections for air and electrical current supplied from a standard 10-volt variable transformer. The overall length is 38 in. (92 cm.) and the diameter just under 0·5 in. (11 mm.)

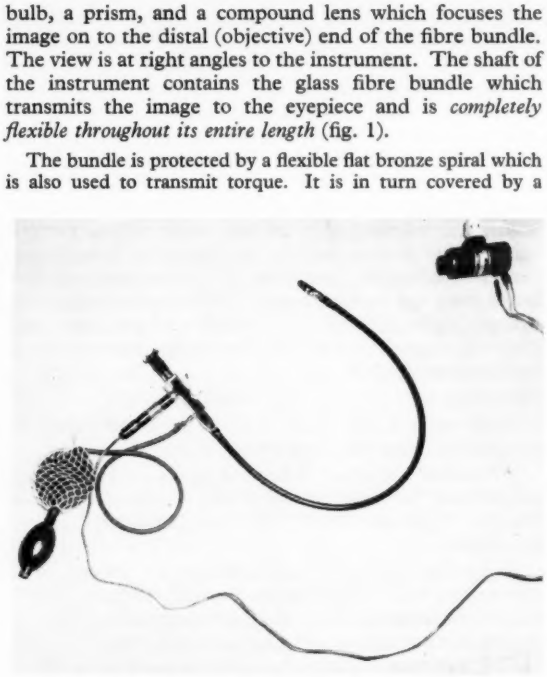

Fig. 1—The fiberscope with air and electrical connections.

The image is transmitted through a bundle of glass fibres traversing the length of the instrument and so arranged spatially that the orientation of the fibres is the same at each end, but, being unbound in the middle, the bundle is completely flexible. Each fibre (diameter 0·0006 in. or approximately 14 μ) transmits a spot of light and the image is transmitted as a composite of these spots of light. About 150,000 fibres are used to make one bundle of about 0·25 in. diameter, allowing high optical resolution. Light transmission through the fiberscope is about $2^1/_2$ times better than through the standard gastroscope, and each fibre is insulated to prevent light scatter from one to another.

The principle of transmission of light through the length of a fibre is that of total internal reflectance which depends on the refraction of light when passing from one optical medium to another of lesser optical density. Light beams are refracted closer to the interface as the angle of incidence becomes smaller. At the critical angle light is refracted along the interface between the two media and at any angle greater than the critical angle, light is reflected back into the medium of origin (in this instance glass). When light enters the end of a rod (or fibre) any light entering at a greater than critical angle (relative to the sides of the fibre) is automatically trapped and perforce has to proceed to the other end of the fibre. Once the light is trapped, curvature or bending of the fibre within wide limits will not cause the light to be lost before it appears at the other end. This briefly is the principle of the instrument used.

Its Clinical Use

Preparation of the Patient

The principal indication for premedication is the prevention of nausea and gagging, rather than analgesia, since the examina-

tion is painless. After trying a variety of drugs for premedication, including promazine ('Sparine'), dimenhydrinate ('Dramamine'), barbiturates and pethidine (demerol), either alone or in combination, as well as examining a number of patients without premedication, the following general method has been adopted. When the patient is first seen the activity of the gag reflex is graded 0, +, or ++. For those with little or no gag reflex, preparation is confined to surface anæsthesia of the throat. Those patients with + gag reflex are given 25–50 mg. pethidine and those with ++ gag reflex are given 50–100 mg. pethidine intravenously 5–15 mins. before endoscopy. The throat is then anæsthetised with spray or gargle of the endoscopist's choice (I have no special preference).

Passing the Instrument

A drop of silicone antifoam * is placed on the tip of the instrument to reduce bubbling (Hirschowitz, Bolt, and Pollard 1954). While an assistant holds the headpiece, the lubricated instrument is passed readily into the stomach with the patient sitting on the side of the bed or couch facing the endoscopist (fig. 2). In no instance has there been any difficulty

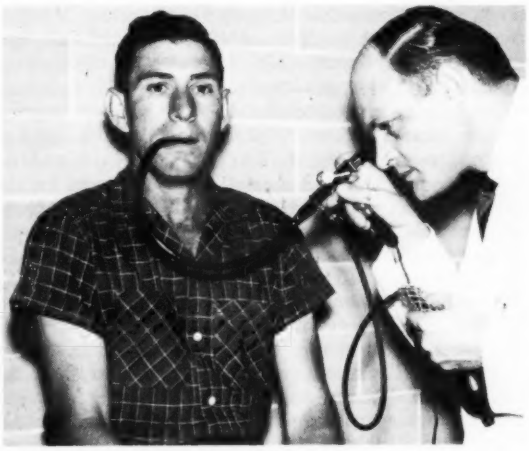

Fig. 2—Stomach of outpatient being examined with the fiberscope.

in entering the stomach, and the blunt end seems preferable to the rubber finger end both for swallowing and for transpyloric passage. Air is pumped into the stomach, as in the standard gastroscopic examination.

Some of the œsophageal mucosa and the whole cardio-œsophageal area can be seen since the focus of the instrument is so arranged to display surfaces in contact with the objective window. By moving the patient into different positions, which can be done without discomfort or danger, a greater area of the stomach can be seen than with the standard gastroscope. The fundus is an area which still cannot be examined, but there are no other "blind" areas. With the patient sitting upright the upper half of the stomach can be seen, but if there is any fluid in the stomach the patient has to lie down on his back or either side for examination of the lower half of the stomach.

Proceeding with the examination, the whole antrum is viewed from a point approximately opposite the angulus on the greater curve. Then, with the patient lying on the right side, the instrument is advanced through the pyloric canal into the duodenal bulb. This has been possible every time it was attempted. The patient is then asked to lie on his back or left side to drain the duodenal bulb.

* Dow Corning.

When there is a gastroenterostomy the instrument can usually, though not always, be passed through the stoma for a distance limited by the respective lengths of the patient and instrument—usually for about 12 in. It is easier to pass the fiberscope into the efferent loop with the patient lying on his back or sitting upright; it is often necessary to advance the instrument into the afferent loop with the patient lying on the right side, and with some help from pressure through the abdominal wall.

Anteroposterior orientation is made relatively easy by observing transillumination through the abdominal wall. Once an organ is distended with air and the light is directed anteriorly, the whole outline of that organ can be readily made out on the abdominal wall. Anatomical sites are readily recognisable when once seen—this applies to the pylorus, duodenal bulb, and the jejunum (see below). Usually the position of the head can be confirmed by observing the outline of the transilluminated organ either jejunum (afferent or efferent loops) or the duodenal cap which is seen to the right of the midline beyond a dark band which represents the pyloric sphincter. The position of the head can also be confirmed by external palpation, and an ulcer can be further identified by finding point tenderness which corresponds to a lesion.

Because of its complete flexibility there is neither discomfort during the procedure nor afterwards. Nearly all the patients examined kept the instrument down for over 20 minutes, some as long as 60 minutes. The patient is not limited to any position, particularly the sword-swallowing one, and spinal deformity or inability to extend the neck no longer preclude examination. The patient can be examined anywhere and our patients have been examined in their beds, in the outpatient clinic, and even sitting in a chair. The instrument is manipulated by pushing and pulling and by rotation of the headpiece from which torque is transmitted to the distal end on a 1:1 ratio by the metal spiral incorporated in its shaft. A certain amount of manipulation can be done through the abdominal wall.

Observations

Œsophagus

Current models of the fiberscope were not designed to provide systematic examination of the œsophagus. Nevertheless, because objects in contact with the objective window can be brought into focus, an adequate view of the cardio-œsophageal area is readily obtained.

Stomach

Body of the stomach (fig. 3).—Resolution of the image is every bit as good as the conventional gastroscope provides, and because of greater light transmission the actual image seen is generally better. Colour reproduction is generally faithful, since transmission of light with wavelength above 5000 Å is close to 100%, being considerably reduced only below 5000 Å. The lesions seen so far include gastric cancer, acute ulcer (fig. 4), chronic ulcer, erosive gastritis, superficial gastritis, gastric mucosal atrophy (in pernicious anæmia), and hypertrophy or mammillation (in duodenal ulcer), and regional enteritis.

Antrum.—The entire pyloric antrum can always be seen and the motility of this area can be studied at leisure since the patient suffers no appreciable discomfort. Close-up views of the sphincter can always be obtained by advancing the instrument into the pyloric canal.

Pyloric canal.—Visible only occasionally with the conventional gastroscope, the pyloric canal can be very readily

examined with the fiberscope. Of particular importance is examination of the lesser curvature of the canal when the question of exact location of an ulcer relative to the pyloric sphincter and of malignancy of ulcers can be answered by direct inspection. Two benign ulcers, which resemble gastric ulcers, have been seen in this series.

Gastroenterostomy stoma (fig. 5).—In a Billroth-II gastrectomy, the stoma behaves very much like the antrum and pylorus in the intact stomach. Contraction waves pass towards the stoma and, unless the stoma is unduly large, close it. The contraction waves are generally not as large nor as well-organised as those at the antrum, being generally asymmetrically circular and larger towards the lesser than the greater curvature. In subtotal gastrectomy the contraction waves appear even less well-organised and are much feebler. It is almost as though propulsive motility waves originate at the angulus and are inherent in the lower part of the stomach. Large stomas which never closed were found in all 3 patients with dumping and bilious vomiting, indicating a possible mechanism for such symptoms.

Normal Duodenal Bulb and Bulbar Sphincter

By far the most important new area accessible to view with the fiberscope is the duodenal bulb or cap. It has been possible to examine the bulb in all 30 patients in whom the manœuvre was attempted.

Passage through the pyloric sphincter is easy to recognise. The bulbar mucosa is a lighter shade of pink than the antrum, and is more succulent than the antral mucosa. Folds of mucosa, generally longitudinal touch each other. Motility consists of circular contractions starting near the base and, becoming circular puckered rings, somewhat like those in the pyloric antrum, follow each other to the apex of the bulb where they close off the lumen in a distinct sphincter mechanism (fig. 6). In some patients the mucosal folds are so succulent that the sphincter itself is not evident and the closed lumen is slit-like rather than circular. Little or no reflux occurs through the closed sphincter.

Vomiting is preceded by obvious reverse peristalsis which appears as circular contractions running cephalad from the second portion of the duodenum and stopping at the bulbar sphincter; at the same time bilious fluid regurgitates into the bulb, and the bulbar contractions, though continuing, do not close the sphincter. Nausea is encountered occasionally when the duodenal bulb is distended with air.

Pathological Findings in the Duodenal Bulb

Deformed duodenal bulb without ulcer.—This X-ray diagnosis is often made and is generally presumptive evidence of ulcer of the duodenum. Three patients with deformed bulbs were examined. The findings were the same in each. No difficulty was encountered in entering the bulb. The shape was vaulted, resembling somewhat the vaginal vault seen through a speculum, and the walls were fairly rigid, flattening anteroposteriorly with compression through the belly wall and then resuming their shape with release of pressure. Mucosal folds were small, being 2–3 mm. high, 1–2 mm. wide, and separated from each other by 3–6 mm. of flat mucosa. They are generally arranged in longitudinal fashion and are irregular. One notable feature of these bulbs was the poor quality of the contractions, which seldom start more than 5–6 mm. proximal to the bulbar sphincter, are much more easily visible, because the overlying mucosa is not so succulent, and end in a very distinct sphincter which opens only partly to about 6–8 mm. and never closes completely. The whole impression is one of rigidity of this area. Mucosal colour is more tan than pink. Deformity of the bulb thus appears to be an endoscopically recognisable entity.

Fig. 7—X-ray of the first acute duodenal ulcer seen in situ by the fiberscope (see fig. 8).

Acute duodenal ulcer.—One such patient was examined twice within an interval of six days. Bleeding had occurred without ulcer symptoms preceding and the X-ray had shown a small crater (fig. 7). The patient was examined two days after bleeding and a small ulcer was seen on the inferior aspect of the bulb just beyond the pyloric sphincter. It appeared to be about 5 mm. in diameter, with a narrow rim of œdema, but no radiating folds, and a black base, presumably a blood-clot. This was the first ulcer seen in the duodenum and luckily could be photographed (fig. 8). The repeat examination showed no ulcer and only a small erythematous spot of œdema to mark the site of the ulcer. The mucosa of the rest of the bulb and the motility were apparently normal. A very similar ulcer was seen in another patient eighteen hours after bleeding. (Figs. 9 and 10 show other acute duodenal ulcers.)

Chronic duodenal ulcer (figs. 11 and 12).—This is the classic small crater with radiating folds seen so often on the X-ray. In one such patient an ulcer was seen in the mid-portion of the anterior wall of the bulb. It resembled very much a small chronic gastric ulcer with a yellow-grey base, sharp borders but ill-defined surrounding œdema and clear radiating folds. Point tenderness over the ulcer could be clearly determined. The remainder of the bulb, while poor in motility, showed only modest abnormalities of the mucosa.

Indolent duodenal ulcer (fig. 13).—One such ulcer was seen in a man with a duodenal-ulcer history of seventeen years. The contrast with the normal bulb, or even the chronic duodenal ulcer bulb, was very striking. The ulcer itself, on the anterior wall, was less well-circumscribed than the usual chronic gastric or duodenal ulcer and much larger than the acute or chronic duodenal ulcer, measuring about 2×1 cm., being roughly élliptical and in the longitudinal axis of the bulb. The base was bluish-grey wet granulation tissue, surrounded by low ridges of rather pink œdema. No new blood-vessels could be seen surrounding this area. The rest of the bulb was deformed, and mucosal folds were low and irregular and in parts appeared macerated. Contractions were weak and ran only a very short distance to a sphincter which did not close. Contractions did not run through the ulcer which extended almost to the sphincter. When the patient was asked to pin-point his ulcer he was able to do so exactly

with his finger. Pressure 1/2 in. away from the ulcer did not elicit pain.

Acute duodenitis.—In a patient with a six-year history of indigestion and alcoholism and a negative X-ray without bulbar deformity the duodenal mucosa was seen to be œdematous and covered with petechiæ and a punctuate yellowish exudate. While being observed an ecchymosis was seen to start in one of the petechiæ and spread submucosally for 4–5 mm. Pressure over the bulb produced tenderness. The lesions were confined to the duodenal mucosa. Re-examination after two weeks showed a return to normal with only 2 or 3 small erosions persisting. Another instance of duodenitis without the petechiæ was observed as a rather red mucosa covered with stringy yellow mucus, but no petechiæ; similar changes were present in the antrum and pyloric canal.

Active chronic duodenitis.—This condition was observed in a patient with a known long history of recurrent duodenal ulceration. The duodenal mucosa appeared macerated, but was not obviously ulcerated at the time of this examination. While not entirely rigid, motility was diminished and occupied only the extreme apex of the bulb near the sphincter. Active ulceration could easily be imagined as occurring in such a mucosa.

Jejunum

Normal appearances.—The jejunal mucosa is somewhat pinker that the gastric mucosa. The jejunal lumen is roughly cylindrical but with external compression is flattened. The mucosal folds are irregularly circumferential but are small and separated from each other. Though enough to get adequate views, the efferent loop does not hold air as long or as well as the stomach, duodenum, and afferent loop for prolonged viewing. No obvious differences were noted in appearance between afferent and efferent loops. The afferent-loop examination can be established by watching the transillumination of the loop through the abdominal wall and by observing bile flowing towards the instrument—in one examination it could be seen issuing from the ampulla of Vater.

Jejunitis.—4 patients have been examined because of symptoms suggestive of marginal or stomal ulceration, but with no demonstrable ulcer. In these patients the gastric side of the anastomosis and the efferent jejunum for a distance of about 1 1/2 in. (2–4 cm.) was obviously red and œdematous with loss of the mucosal ridging. 2 patients had superficial exudate in this area and external compression of the area in view of the fiberscope elicited tenderness. While many such cases are reported as normal on X-ray, repeat examination after three to six weeks of ulcer treatment reveals a return of the mucosal pattern due apparently to subsidence of œdema at the stoma. Jejunitis without ulcer seems to be a fairly common cause for recurrent pain after gastrectomy.

Jejunal ulceration.—Because the ulcer is in the efferent loop and often hidden by swelling around the stoma, conventional gastroscopy seldom allows display of marginal ulcers. The fiberscope, however, allows examination of the ulcers much more closely and certainly from beyond the stoma. One such instance was encountered.

Discussion

The application of fibre optics to the examination of the upper gastro-intestinal tract has opened new dimensions in diagnostic endoscopy. Areas not previously accessible are now readily displayed—the pyloric canal, the duodenal bulb, and both afferent and efferent loops of the jejunum through the gastroenterostomy stoma. These areas can not only be studied for abnormalities but also for motility for comparatively long periods. Furthermore, the complete flexibility of the fiberscope means that examination is very much easier for the patient, and introduction of the instrument requires no special skill. More important, damage to the œsophagus or stomach, particularly the œsophagus, is no longer a consideration as it was with the conventional gastroscope. Thus, many more patients can be examined easily and safely and the indications for its use should be much broader. Among the areas where the instrument will be particularly valuable are in diseases of the duodenal bulb, the post-gastrectomy syndromes, and in the direct photographic recording of motility of the upper gastrointestinal tract for periods long enough to be meaningful. The early examination of the upper gastrointestinal tract in bleeding will lead to more precise diagnoses and far fewer patients will leave hospital with upper gastrointestinal bleeding unexplained.

Several extremely interesting observations have been made in the duodenal bulb. For one, a sphincter at the apex of the bulb has been clearly seen, and corresponds to the radiological apex. It seems to represent an area where sphincteric motility of the upper gastrointestinal tract stops, and may well have something to do with the localisation of ulcers in the bulb. The attempted classification of duodenal ulcers into acute, chronic, and indolent seems to have some merit in terms of prognosis and possible surgery. It is the indolent ulcer that seems to be the "incurable" ulcer, and judging simply from the appearance of the mucosa of the bulb it would be more correct to consider ulceration as a recurrent episode in an incurable disease of the mucosa of the bulb.

Another syndrome which will bear much closer study is the one of jejunitis after gastrectomy, clinically resembling marginal ulceration with pain and slow bleeding and which responds to ulcer therapy. It remains to be seen whether stomal ulceration is part of this syndrome.

It may be stated unequivocally that the fiberscope has already reached the stage where it should replace the conventional gastroscope. We would no longer consider using the old instrument.

Summary

A completely flexible optical instrument employing fibre optics has been used successfully to examine the œsophagus, stomach, duodenal bulb, and both afferent and efferent jejunal loops through gastroenterostomy stomas. It has the advantages of easy passage, safety, and comfort to the patient. Image resolution is every bit as good and light transmission 2 1/2 times better than with the conventional gastroscope, making possible adequate colour photography without additional illumination. The conventional gastroscope has become obsolete on all counts. Among the observations made so far are: the finding of a distinct sphincter at the apex of the duodenal bulb; the recognition of three types of ulcer (acute, chronic, and indolent); and a syndrome of postgastrectomy jejunitis in patients with the clinical picture of marginal ulceration but without the ulcers.

The colour pictures were taken with an Exakta Varex II single-lens reflex camera with a 58 mm. lens coupled to the eyepiece of the fiberscope; the film is super-Ektachrome, ASA 160, at 1/2 sec. exposure. More than 60% of exposures taken are adequate. The photographs are not as sharp as the visual image, partly because of the long exposure time and partly because the ocular lens was designed for the eye rather than the camera. Minor improvements will, however, make sharp still and motion pictures part of any fiberscope endoscopy.

Production of the working model of the fiberscope for examination of the upper gastrointestinal tract is the result of hard, patient, and

frequently inspired work of Mr. L. E. Curtiss and Dr. C. W. Peters (who have been concerned in this project since its inception), as well as that of Dr. John Hett, with the unflagging optimistic support of Mr. F. J. Wallace, president of American Cystoscope Makers, Inc., Pelham Manor, New York, where the most recent work has been done, and from whom instruments may be obtained.

REFERENCES

Hirschowitz, B. I., Curtiss, L. E., Peters, C. W. (1958) *Gastroenterology*, **35**, 50.
— Bolt, R. J., Pollard, H. M. (1954) *ibid.* **27**, 649.

A NEW CONCEPT OF CAPILLARY CIRCULATION IN BONE CORTEX

Some Clinical Applications

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With illustrations on plate

ONE of us (Heald 1951) described an intensive study of 200 refractory cases of pain, of a type then called fibrositis. Many of these patients were treated by injections of oily solutions of salicylate deep into the muscles, some by injections into the periosteum, and some by injections into the bony cortex. Because the late Dr. Laughton Scott found that salicylate injections into the bony cortex were effective, this technique was studied further by Mr. L. W. Plewes and one of us (C. B. H.). The results were good, and encouraged further work.

A " spray-like effect " in muscles was discovered during these investigations. This is the name given to the radiological appearance following the injection of radiopaque oil into the neighbouring bone. Two of us (R. G. H. and M. B.) then began to investigate the anatomical background of this phenomenon; and we have been led to a new concept of the nature of circulation through bone cortex. Further work on treated cases was done by one of us (A. C. E.) in cases of painful-shoulder syndrome which had been resistant to other treatment. They were all cases of the supraspinatus-tendon rotator-cuff type, which had previously improved after injection into the bone of a salicylic-acid preparation. By adding an equal amount of 'Hypaque' to the injection the track followed by the injection material could be studied. Continued clinical improvement was obtained in these patients.

Injection and Its Results

The injection consisted of 0·1% salicylic acid, 0·5% procaine, and 2% urea. To this was added an equal volume of hypaque. After the skin and periosteum had been anæsthetised with procaine, a special trocar needle was tapped into the cortex of the acromion process (fig. 1). This is not painful if the periosteum is infiltrated with 0·5% procaine.

The injection must be made into an area where there is a direct attachment (not a tendinous insertion) of muscle-fibres to the periosteum. A radiograph was taken with the needle in situ, 2·5 ml. of the solution injected, and a further film taken. There is a sharp pain at the moment of injection, but this subsides almost at once. Surprisingly little force is needed to inject the solution. The position of the needle in the bone and the " spray effect " produced are shown in fig. 1.

The " spray effect " was most noticeable in younger subjects, and was less obvious in an older patient who had considerable sclerosis of the acromion process. In this series, the radiological appearances of the " spray effect " were identical with those produced in 1951.

The technique was repeated (R. G. H. and A. C. E.) on the body of a man aged 67, who had died only 6 hours before from carcinoma of the œsophagus. A mixture of hypaque and indian ink was used so that the result could be studied both radiologically and histologically; and observations were made on both acromion processes and the lateral epicondyles of the humeri.

After confirming radiographically that a " spray effect " was obtained (figs. 2 and 3), the pieces of bone into which the injection had been made were removed together with a large part of the attached muscles, fixed, embedded in low-viscosity nitrocellulose, and a histological examination was made. Low-power microscopic investigation showed that the indian ink occupied the interfascicular spaces of the attached muscles in both cases (fig. 4). The needle had perforated the compactum of the acromion process, but not that of the lateral epicondyle. The diameter of the hole (fig. 5) was 0·3 mm., whereas the diameter of the needle was 1·0 mm. The indian ink had passed into the sinusoids of the cancellous bone in only a small quantity at both sites of injection, and had clearly not even had an opportunity of doing so in the lateral epicondyle.

In the acromion process the hole made by the point of the trocar of the injection needle was smaller than the orifice of its cannula, so hindering the passage of medium into the underlying bone. The path followed by the injection material was mostly from the orifice of the needle cannula into the periosteum, and from here into interfascicular spaces of adjoining muscle. The observed centrifugal spread of the injected

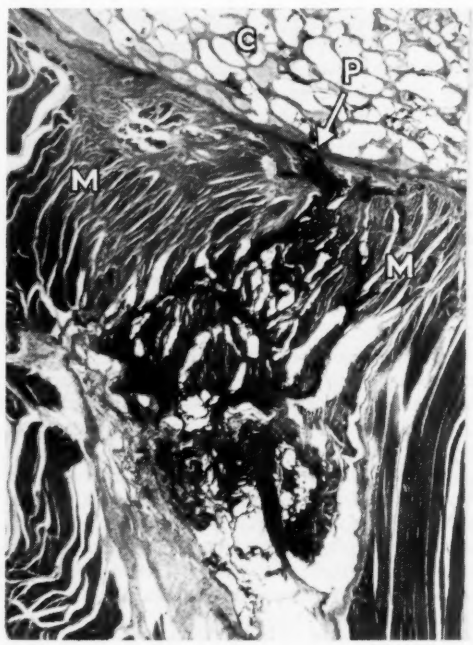

Fig. 4—Section through cortex (C) of acromion process and attached muscle (MM) of deltoid after injection of hypaque and indian ink.

This tissue was removed immediately after taking the radiograph in fig. 2. The site of perforation (P) of the compactum, and the filling of the interfascicular spaces of the deltoid by indian ink radiating from it, are clearly visible. Hæmatoxylin and eosin (×3·5).

material in vivo is only compatible with an outward flow of blood from bone into muscle. That this is the case is supported by our anatomical studies.

Ideas on Vascularisation of Bone

The classical concept of bone vascularisation, based on the exposition of Testut and Latarjet (1948), is represented in fig. 6. Certain facts are not in accord with this explanation. The vessels of the cortical vascular mesh are all simple endothelial tubes and cannot be recognised histologically except as capillaries, one for each canal (Weidenreich 1923, Ham 1953, Brookes 1960a). If, as previously assumed, blood emptied into the cortical capillary bed from both periosteal and medullary aspects, the mechanism of venous drainage of the cortex remains unexplained: the blood in the capillaries cannot go both ways, centripetally from the surface and centrifugally from the marrow.

Fig. 5—Hole (H) produced in compactum of acromion process at site of perforation (P) shown in fig. 4. A bony spicule (S) in the subjacent cancellous bone has been displaced. H. & E. (×40).

Fig. 7—Oblique section through diaphysis of femur of rat, injected intravascularly with indian ink, showing the medullary vascular bed (M) and cortical capillaries emanating from it in profusion. H. & E. (×45).

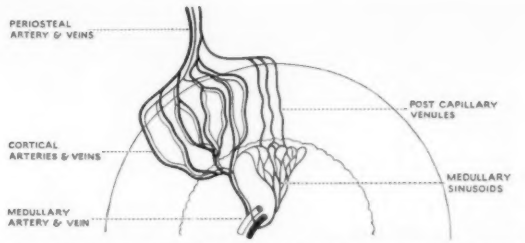

Fig. 6—Inaccurate classical concept of bone vascularisation, based on Testut and Latarjet (1948), demonstrated diagrammatically in a transverse section of a long bone.

By means of hæmodynamic experiments and microradiographic analysis, Brookes and Harrison (1957) and Brookes (1958a and b, 1960a and b) have shown that in man and other mammals arterial blood from the periosteum does not normally pass centripetally into bone cortex. Arterial blood is delivered to the compactum by means of a medullary arterial system composed of anastomosing branches of the principal nutrient artery and the arteries of the bone extremities. The blood-flow in cortical bone passes centrifugally from the medullary arterial system into the cortical capillary mesh (fig. 7), and out into the capillaries of the periosteal membrane, and the interfascicular capillaries and veins of attached muscles (fig. 8).

Brookes and Harrison (1957) have also shown that the cortical capillary mesh communicates, not only with the

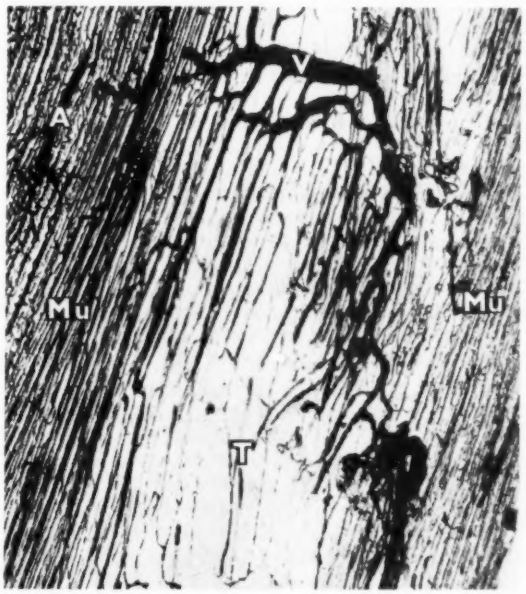

Fig. 8—Oblique section through tibia of rat injected intravascularly with indian ink.

The continuity of the cortical capillaries (T) with interfascicular capillaries and venules of attached muscle (Mu) is well shown in this preparation. The venule V is to be compared with the small artery A seen breaking up into a leash of tortuous arterioles and capillaries. H. & E. (×50).

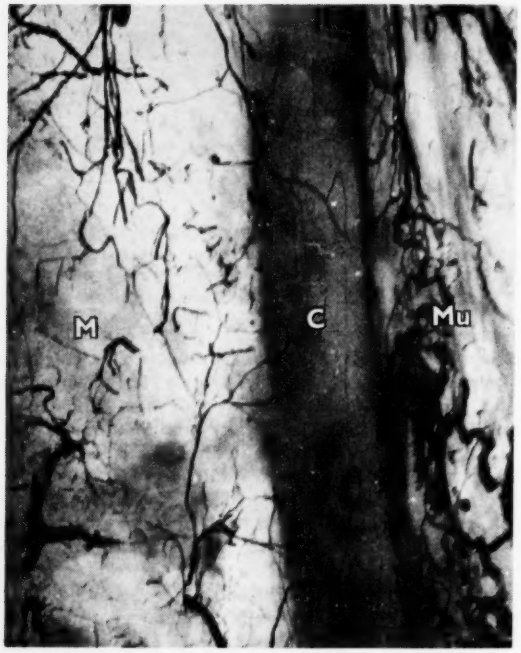

Fig. 9—Microradiograph of longitudinal section through diaphyseal cortex of normal human tibia (limb arteries injected with barium sulphate suspension).

Medullary arteries (M) are shown giving rise to fine terminals passing centrifugally into the cortex (C). No centripetal penetration of barium sulphate has occurred from the arteries of the periosteum and adjacent soft tissue (Mu). (×4.)

capillaries outside the bone, but also internally with the sinusoids of the marrow. These do not unite medullary arteries to the veins said to accompany them (Langer 1876), but form the distinctive vascular bed of the marrow. This is connected to a longitudinally disposed central venous sinus of large calibre, and to the cortical capillary bed. Medullary arteries feed into the sinusoids of the marrow.

The microradiographical technique of Brookes and Harrison (1957) was used, not only to display the vascular anatomy of bone, but also to determine the direction of the blood-flow in the cortical capillaries. Brookes and Harrison (1957) first showed that the barium-sulphate suspension used by them for intravascular injection did not fill the capillary bed but could just enter into it. In normal material the injection mass passes into bone cortex from the medulla, but not from the periosteum (fig. 9). This provided good confirmatory evidence for a centrifugal blood-flow in the cortical capillaries.

Fig. 10 represents diagrammatically the new concept of bone vascularisation, based on the work of Brookes and Harrison (1957). This is a modern version of the original Haversian hypothesis of centrifugal bone nutrition. The plan of cortical vascularisation in figs. 10 and 11 shows that the blood-flow may be reversed, if the *vis a tergo* of medullary arterial pressure should fall. Brookes (1960a and b) has shown that when the arterial blood-flow to the medulla is curtailed, either in peripheral occlusive vascular disease in man, or experimentally in the rabbit, there is compensation for the resultant ischæmia of bone. This compensation is achieved in part by a centripetal flow into the cortex from the external soft tissues. A centripetal periosteal blood-supply to bone (fig. 12) is therefore of importance to bone nutrition only in ischæmic conditions, when it assumes the role of a collateral blood route. This is related to the severity and chronicity of the ischæmia.

Both clinically and experimentally, Brookes (1960a and b) found that ischæmic bones became radiologically and histologically osteoporotic. The osteoporosis is a true one —i.e., it is not a halisteresis with a leeching-out of the bone salt. The fundamental bone substance appeared unaltered in constitution, but the vascular canals enlarged considerably, and contained multiple blood-vessels, probably the result of the disturbed and irregular circulatory conditions in the cortex.

Discussion

That arterial ischæmia produces osteoporosis in peripheral occlusive vascular disease is well known (Müller 1926, Jaffe and Pomeranz 1934). Some other types of clinical osteoporosis are explained by Brookes (1960a) as the result of ischæmia of bone. In certain circumstances osteoporosis may be due to a disturbance of the

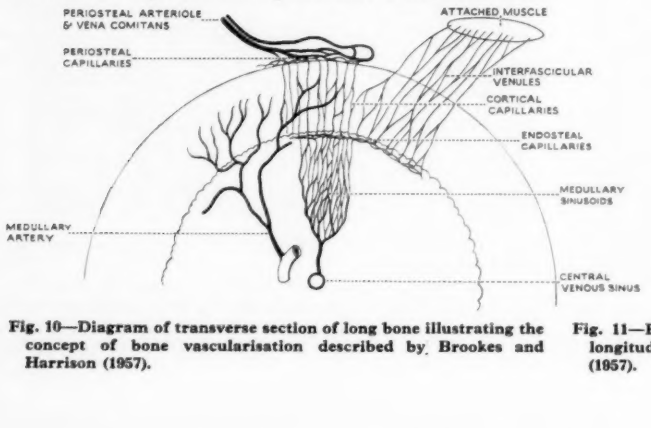

Fig. 10—Diagram of transverse section of long bone illustrating the concept of bone vascularisation described by Brookes and Harrison (1957).

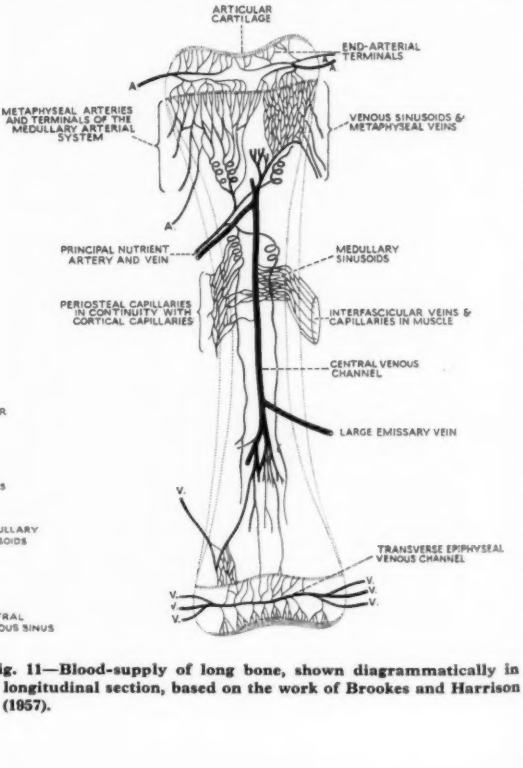
ARTICULAR CARTILAGE
END-ARTERIAL TERMINALS
METAPHYSEAL ARTERIES AND TERMINALS OF THE MEDULLARY ARTERIAL SYSTEM
VENOUS SINUSOIDS & METAPHYSEAL VEINS
PRINCIPAL NUTRIENT ARTERY AND VEIN
MEDULLARY SINUSOIDS
PERIOSTEAL CAPILLARIES IN CONTINUITY WITH CORTICAL CAPILLARIES
INTERFASCICULAR VEINS & CAPILLARIES IN MUSCLE
CENTRAL VENOUS CHANNEL
LARGE EMISSARY VEIN
TRANSVERSE EPIPHYSEAL VENOUS CHANNEL

Fig. 11—Blood-supply of long bone, shown diagrammatically in longitudinal section, based on the work of Brookes and Harrison (1957).

pumping action of attached muscles. This follows from the continuity of cortical capillaries with interfascicular capillaries. The pumping action of muscles in maintaining the normal cortical circulation may well be considered of clinical importance, since it provides an explanation for a variety of osteoporotic lesions. Examples occur in fracture, immobilisation, muscle paralyses, anterior poliomyelitis, hemiplegia, trauma of nerve cords and plexuses, disseminated sclerosis, and other damage to the central nervous system. Osteoporotic lesions may also be seen in diseases of joints where stiffness or fixation hamper the normal direct pumping action of muscles on bone.

Other factors besides circulatory deficiency are, of course, significant causes of osteoporosis. Glandular dystrophy is of undoubted importance in the osteoporosis of pregnancy, diabetes mellitus, Cushing's syndrome, and acromegaly. Even in this group of disorders, however, the osteoporotic lesion may well be a result of a disturbance of the normal permeability of the vascular endothelium of bone. It is across this endothelial wall that the raw material for bone construction must be transported. In mice undergoing massive œstrogen treatment, the marrow blood-vessels provide a scaffolding around which endosteal bone can form (Brookes and Lloyd 1960). The disturbance of vascular permeability in menopausal and dystrophic osteoporoses may have a similar ætiology (Ranney 1959).

These investigations on the vascularisation of bone suggest that a reorientation of clinical thought is necessary. The fact that the blood-vessels of the marrow contain blood which plays a part in the nutrition of bone cortex, periosteum, and tissues near it, implies the existence of a centrifugal circulation. In our view, tissues adjacent to bone have a direct connection with the hæmopoietic and other elements of bone-marrow. Not only does this explain the cause of some types of osteoporosis, but it may also help to elucidate the clinical phenomena of " painful shoulder "and similar conditions.

Fig. 12—Microradiograph of longitudinal section of human tibia taken from limb amputated for peripheral occlusive vascular disease, showing type of cortical vascularisation found in ischæmic and osteoporotic bone.

The cortical vessels (C) are irregular in calibre; many have undergone considerable expansion. A normal centrifugal blood-flow in the cortex from the medulla (M) has been in part replaced by a pathological centripetal circulation from the periosteum. (×4·5.)

Summary

Clinical, experimental, and histological evidence shows that, during most of adult life, the blood-flow through bone cortex runs in a centrifugal and not in a centripetal direction, as has been taught hitherto.

The clinical implications of this finding are discussed.

This work was aided financially by the Sir Halley Stewart Trust. We are indebted to Colonel Basil Blewitt, Newsham General Hospital, Liverpool, for providing facilities for injections in a cadaver; to Mrs. M. Barrett, Mr. L. G. Cooper, Mr. A. Taunton, and Mrs. C. Morley for technical assistance; to Mr. D. J. Kidd for help with the drawings; to Mr. L. Reeve for the photographs; and to Dr. D. E. Olliff for help in the preparation of this paper.

REFERENCES

Brookes, M. (1958a) *J. Anat., Lond.* **92**, 261.
— (1958b) *Anat. Rec.* **132**, 25.
— (1960a) *J. Bone Jt Surg.* **42B**, 110.
— (1960b) *J. Anat., Lond.* (in the press).
— Harrison, R. G. (1957) *ibid.* **91**, 61.
— Lloyd, E. G. (1960) *ibid.* **94**, 286.
Ham, A. W. (1953) Histology. Philadelphia.
Heald, C. B. (1951) *Trans. med. Soc. Lond.* **67**, 5.
Jaffe, H. L., Pomeranz, M. M. (1934) *Arch. Surg., Chicago*, **29**, 566.
Langer, K. (1876) *Denkschr. Akad. Wiss. Wien*, **36**, 1.
Muller, W. (1926) *Arch. klin. Chir.* **142**, 610.
Ranney, R. E. (1959) *Endocrinology*, **65**, 594.
Testut, L., Latariet, A. (1948) Traité d'Anatomie Humaine. Paris.
Weidenreich, F. (1923) *Arb. anat. Inst., Wiesbaden*, **69**, 382.

INTERMITTENT CLAUDICATION OF THE CAUDA EQUINA

An Unusual Syndrome Resulting from Central Protrusion of a Lumbar Intervertebral Disc

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With illustrations on plate

IN 300 consecutive cases of lumbar-disc protrusion we have seen 6 patients in whom the presenting symptoms have been intermittent pain and paræsthesia in the legs, related quantitatively to exercise.

The syndrome seems to be due to a temporary and recurring disturbance of the blood-supply to part of the cauda equina which improves after a short period of rest. Though we appreciate that the cauda equina cannot itself " limp ", we suggest that the term " intermittent claudication " is suitable and compares with that of " intermittent claudication of the spinal cord " given by Dejerine (1911).

A typical history is described in detail, and the salient features of all 6 cases are shown in tables I–IV.

A Typical Case

A company director (case 1) aged 68, when he finally came to surgical treatment, said that his symptoms had started some eight years before, when the sensation of " pins-and-needles " developed in his feet after standing or walking for from ten to twenty minutes. He was seen at another neurological centre at that stage, when the only abnormal neurological sign was an

absent left ankle-jerk. A blood-count excluded a macrocytic anæmia and he was thought to have peripheral vascular disease as the pulses were felt only with difficulty; he was treated with injections of tolazoline hydrochloride ('Priscol') for six months without any benefit. He was later admitted to the same hospital when the physical signs were unchanged, except that the left plantar response was now thought to be doubtfully flexor.

The lumbar cerebrospinal fluid (C.S.F.) contained 40 mg. of protein per 100 ml., but a myelogram showed an almost complete obstruction at a level which corresponded to the lumbar 4/5 intervertebral disc. No surgical treatment was undertaken.

His symptoms persisted for another year, and then there was a spontaneous and inexplicable remission for three years, after which his dysæsthesiæ gradually returned. At that time

TABLE I—PRODUCTION OF SYMPTOMS OF INTERMITTENT CLAUDICATION OF CAUDA EQUINA

Case	Age	History (yr.)	Distance producing symptoms	Time in which obtained relief
1	68	(8) 4	1/8–1 mile	1 min.
2	51	6	1 1/2 miles reducing to few yards	2–3 min.
3	55	4	50 yards	Seconds to 2 min.
4	49	2	Variable 800–100 yards	"A short time"
5	64	1/2	50–100 yards	Few min.
6	54	(7) 6	1 mile	30 sec.

Figures in parentheses indicate the time of onset when symptoms were related irregularly to the amount of exercise (see text).

paræsthesiæ and numbness appeared after walking about three-quarters of a mile, and extended from his feet up the calves into the thighs, and if he persisted in walking these sensations extended to involve the buttocks, perineum, urethra, and base of the penis, and were accompanied by a feeling of "blunt knives sticking into the lumbar region and buttocks". When these symptoms were fully developed he was able to appreciate distension of the bladder, but not the passage of urine down the urethra. At the same time his walking became difficult owing to unsteadiness and lack of balance. If he stopped walking the paræsthesiæ, pain, and numbness cleared completely within a minute, and he would then be able to carry on for a further period, when the process was repeated. Between these paroxysms the legs felt perfectly normal.

His symptoms persisted without change until 1958, when he was admitted to the Middlesex Hospital. His blood-pressure was 120/80 mm. Hg, and the peripheral pulses in the legs were just palpable. Straight leg raising (S.L.R.) was to 80° on each side; there was no wasting in the lower limbs; the knee-jerks were normal, but the right ankle-jerk was reduced and the left absent. The right plantar reflex was flexor, and the left

TABLE II—NEUROLOGICAL SIGNS

Case	S.L.R.	Wasting	Reflexes	Analgesia		Anæsthesia	
				Rt	Lt	Rt	Lt
1	80° 80°	Nil	K.J. + + A.J. + O P.R. F ?E	Nil		Nil	
2	90° 90°	Feet, calves, glutei, hamstrings	K.J. + + A.J. O O P.R. F F	s1	s3-5	s1–s5	s1–s5
3	90° 90°	Nil	K.J. + + A.J. O O P.R. F F	(L5)	(L5)	(L5)	(L5)
4	85° 85°	Left calf	K.J. + + A.J. + O P.R. ?F ?F	Nil		Nil	
5	90° 90°	Nil	K.J. + + A.J. O O P.R. F F	Hyperæsthesia L5–s1	L5–s1	Nil	
6	70° 80°	Both thighs; calves + rt. buttock	K.J. + + A.J. O O P.R. F F	Nil		(s1)	(s1)

K.J. = knee-jerk. + = present. E = extensor.
A.J. = ankle-jerk. O = absent. F = flexor.
P.R. = plantar response. S.L.R. = straight-leg raising. Rt = right. Lt = left.
Figures in parentheses indicate impairment; figures without parentheses indicate loss.

TABLE III—INVESTIGATIONS

Case	Plain X-rays lumbar spine	C.S.F. protein (mg. per 100 ml.)	Level of myelographic block
1	Degeneration L1/2, L3/4, L4/5, slight forward displacement L3 on L4 (6 lumbar vertebræ)	40	L4/5
2	Narrowing L2/3, L3/4, slight forward displacement L4 on L5	75 + 30 *	L4/5
3	Minimal narrowing L3/4	170 + 100 *	L3/4
4	Normal	100	L3/4
5	Considerable spondylotic changes	120	L3/4 + L4/5
6	Normal	30	L4/5

* 2 results indicate findings on separate occasions.

indeterminate. There was no sensory loss. After he had walked for ten minutes both knee-jerks became depressed, and did not return to their previous state until he had rested for from three to five minutes.

Radiographs of the lumbar spine showed 6 lumbar vertebræ with degeneration at the L1/2, L3/4, and L4/5 intervertebral discs and slight forward displacement of the body of L3 on L4. An aortogram excluded the presence of angiomatous malformation of the spinal cord, and showed a normal aorta. A cisternal myelogram revealed an almost complete obstruction at the L4/5 disc level, with only two droplets of 'Myodil' passing onwards when the patient was in the extreme upright position. Superimposed on the pool of obstructed myodil was the appearance of thickened nerve-roots (fig. 1).

A full laminectomy of the L4 and L5 vertebræ was carried out, and when the arch of L5 was removed the dura bulged through

TABLE IV—OPERATION AND RESULTS

Case	Operation	Postoperative state
1	Large transverse spondylotic bar, L 4/5, bony hard, irremovable; decompression	"A joy to walk"—1 year
2	Whole width of L4/5 disc protruded backwards, partly removed	Could walk 2 miles and worked 8 hours a day as a labourer—7 years
3	Narrow spinal canal, large central disc protrusion L3/4; completely removed	Worked 2 years as a farm worker before suddenly having L5-root lesion
4	Narrow spinal canal, disc protrusion L4/5, size of pea; completely removed	Complete recovery, worked as a labourer lifting 1/2 cwt. 2 years required lumbar corset for backache. Later cardiac failure
5	No operation	No operation—spontaneous recovery back to general practice
6	Large soft disc protrusion L4/5; completely removed	Returned to work as a factory hand; symptom-free 5 years later

under tension and a large transverse spondylotic bar from the L4/5 disc was found anteriorly. At the site of this indentation the theca was observed to have been compressed firmly backwards against a thick ligamentum flavum. The dura was white, indurated, and thickened over the apex of the compression. The anterior bony protrusion could not be removed, and surgical treatment was limited to a large posterior decompression.

Two months after operation he could walk as far as he wished without pain or numbness, and the ankle-jerks had returned to normal. Four months later he wrote: "I now enjoy walking and standing after many years of walking and standing only when I could not avoid it, then with pain and numbness most of the time, and always with considerable discomfort."

Symptoms

Pain and paræsthesiæ in the distribution of the lower lumbar or sacral dermatomes on walking a certain distance were characteristic features shown by all 6 patients. The sensations were described typically as "pins-and-needles", usually painful and burning, starting in the feet and extending up the calves into the lower thighs. In some cases the sensation extended into the gluteal region, perineum, and even the urethra. The paræsthesiæ were commonly felt simultaneously in both lower limbs, often more pro-

nounced in one than the other; but they sometimes appeared first in one leg and later spread to the other (fig. 2). The symptoms, when fully developed, usually had a constant relation to *walking a certain distance*, though in one of the patients they also arose after standing for some fixed length of time. They were *relieved completely after a half to three minutes by standing still or by sitting down* (table I). The sensations would reappear after the patient had resumed walking and had covered a similar distance. 2 of the patients (cases 1 and 2) found that if they persisted in walking despite these symptoms, the legs became weaker as well as unsteady and lacking in balance, and the second patient described his gait in these circumstances as " waddling ".

In the early stages of the condition the quantitative relationship of the paroxysmal dysæsthesiæ to exercise was sometimes variable, and the symptoms might appear only at intervals; 1 patient had, in fact, a complete remission for three years. Once the condition was fully developed, however, the relation of symptoms to exercise was constant, except in 1 patient (case 4).

In some patients, areas of the skin over the feet or lower part of the legs were the site of persistent tingling or numbness, which was overshadowed by the appearance of the burning sensation on exercise, and was felt again when the burning sensation disappeared on resting. It should be emphasised that none of these patients had sciatic pain, and there were few symptoms which might have drawn attention to the intervertebral disc being the cause of the condition. 1 patient complained of low back pain, and another had had a single attack of sciatica, fourteen years before his intermittent symptoms began.

Neurological Signs

Examination of the central nervous system in these patients always showed some evidence of involvement of the nerve-roots of the cauda equina, though in some patients this was very slight. If attention tended to be focused on peripheral vascular disease, it was understandable that the neurological signs might easily be overlooked. The abnormal signs, however, varied from one extreme of the neurological spectrum to the other (table II).

Case 2 had an obvious cauda-equina syndrome shown by bilateral wasting and weakness of the glutei, hamstrings, and calf muscles, with hypalgesia and hypæsthesia in all the sacral segments, combined with disturbed bladder function. On the other hand in case 1 the signs were so slight—consisting solely of reduced ankle-jerks and an equivocal left plantar response—that in the presence of poor peripheral pulses in the legs, the neurological signs were ignored and treatment for vascular disease was continued for some seven years.

Signs conspicuous by their absence were those associated with lateral protrusion of an intervertebral disc; in particular, limitation of S.L.R., which was full in 5 patients and only slightly reduced in 1; and in all patients spinal movements were full except 1 (case 3), where they were painlessly restricted owing to extensive spondylosis.

Investigations and Treatment

Plain radiographs of the lumbar spine were normal in 2 patients (cases 4 and 6), there was mild narrowing of the affected disc in another (case 3), and in the remaining patients there were generalised spondylotic changes also involving the relevant disc, with some narrowing. In none was there gross narrowing of the affected disc (table III).

Spinal Puncture and Myelography

The protein content of the lumbar C.S.F. was high (75–170 mg. per 100 ml.) in 4 cases. This increase of protein depended usually on the site of the lumbar puncture in relationship to the block. Interestingly, in the remaining 2 patients, normal cerebrospinal fluid was obtained, manometric findings being normal because the needle was in each case inserted unwittingly at a level higher than that of the protrusion.

Fig. 1—Case 1: Myelogram showing hold-up at L4/5 disc space with sinuous filling defects above corresponding to congested and thickened cauda-equina nerve-roots (confirmed at operation). Two drops of myodil are passing to the left of the obstruction. (There are 6 lumbar vertebræ with spina bifida of the 6th.)

In all 6 patients the diagnosis finally depended on the myelographic findings. The appearances were characteristic, and consisted of a block to the myodil column at the level of an intervertebral disc, and was almost complete; a few drops might pass round the side of the obstruction if the patient was put in such a position that gravity exerted its full force. In those cases where the myodil had been inserted above the block, all the contrast material was seen to have collected in the sacral sac after the lapse of a few hours to a few days (fig. 3). A pathognomonic feature of the myelogram was the demonstration of thickened nerve-roots superimposed on the obstruction (figs. 1, 4, and 5).

The appearance of a localised block at the level of an intervertebral disc with evidence of swollen roots has been

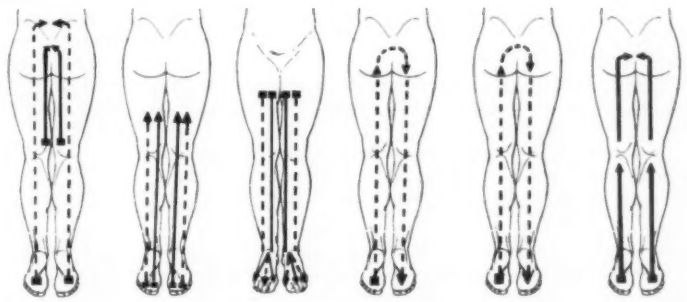
Case 1. Numbness and severe pain.
Case 2. Numbness and painful sensations.
Case 3. Pins and needles followed by pain.
Case 4. Numbness only.
Case 5. Pins and needles.
Case 6. Burning pain.

Fig. 2—Distribution of dysæsthesiæ: continuous lines indicate painful sensations, interrupted lines indicate painless sensations.

described by Lewtas and Dimant (1957) in 2 cases. They considered the condition to be "hypertrophic interstitial polyneuritis" of the cauda equina, but it would seem from the details given that their patients—in particular, their second patient in whom "walking would bring on the pain"—may well have been suffering from the condition described here.

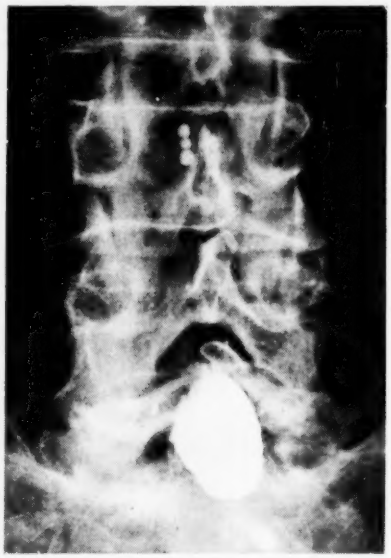

Fig. 3—Case 1: Myodil in lumbar sac some days later.

Findings at Operation

A laminectomy at the site of the myelographic block was performed on 5 out of the 6 patients and an anterior disc protrusion was found in all 5 of them, ranging from a hard bony bar to a soft degenerate protrusion (table IV). The dura was tense and white, and there was a severe localised arachnoiditis with œdema and thickening of the intrathecal nerve-roots, which were fused over a distance of 2–3 cm. into a solid flattened bundle. The latter was usually adherent through the theca both to the apex of the protrusion and often posteriorly to the ligamentum flavum, so that the roots of the cauda equina could not escape the firm and inexorable pressure of the protruded disc.

4 patients had part or the whole of the disc protrusion removed, but in the 5th it could not be removed because of its bony consistence.

Postoperative Course

All the patients who were operated upon were entirely relieved of intermittent dysæsthesiæ and pain; and all returned to work, including 2 labourers and a farm hand. They were able to walk in comfort for any distance they wished in the follow-up period which ranged from six months to seven years.

Case 2, with a severe cauda-equina syndrome, still had motor and sphincter disturbance although this was less than before operation.

Two years after operation 2 patients had new symptoms of lumbar spondylosis: low back pain in 1, which was alleviated by a lumbar corset; and a complete motor and sensory L5-root lesion in the other.

Pathology

These 6 patients illustrate a syndrome in which there is compression of the nerves of the cauda equina produced by a central disc protrusion. It occurred in 2 patients at the L3/4 disc, at the L4/5 level in 3, and at both the L3/4 and L4/5 levels in the remaining patient (table III). There seems, however, no reason why a similar protrusion at any of the other lumbar-disc levels should not produce intermittent symptoms, which would differ solely in the extent of the cauda equina involved. The protrusion seems to develop slowly and insidiously, the usual signs associated with lateral disc protrusion being absent.

The essential feature in the production of these intermittent symptoms was shown at operation to be an unyielding compressive disc, for the condition is not found with soft and more diffuse compressions, such as are caused by the common tumours (neurofibroma and ependymoma) in the lumbar spinal canal. The segmental emergent lumbar roots in their dural sheaths tended to be lateral to the protrusion in each case, thus escaping most of the pressure; hence, sciatica, with signs of "tension" in the leg and spine, was not produced in any of the patients.

Pathophysiology

Here the term "compression" of the nerve-roots is used solely descriptively and implies altered conduction in the nerves associated with a static mechanical pressure without specific reference to the underlying pathological mechanism, which still remains uncertain. It has been shown that nerves are particularly sensitive to angulation and also to interference in their intrinsic blood-supply, but not to evenly distributed stretching or compressing forces (Denny-Brown and Brenner 1944). Which of these mechanisms is responsible is still not known and the question will not be pursued further.

The *persistent* and unvarying background symptoms of paræsthesiæ and numbness of the feet and legs, with the associated neurological signs present in some of the patients, can be explained by mechanical compression of the cauda-equina nerve-roots, but a static mechanism will not account for the *intermittent* symptoms. A dynamic factor must be operative and two mechanisms need to be considered—mechanical and vascular.

Mechanical Factors

When a person stands up there is an increase in the weight borne by the lumbar vertebræ and the intervertebral discs, and a disc protrusion may bulge a little more and compress the adjacent nerve-roots more firmly, as can sometimes be shown at myelography. This mechanism, however, cannot account for the intermittent symptoms described here, since these occur only as a result of walking and the essential feature for relief is the cessation of this exercise, there being no need to lie down.

Furthermore, the disc protrusion in 1 patient (case 2) was found at operation to be of bony hardness and hence quite incapable of further protrusion in response to weightbearing.

A mechanical explanation is favoured by some Dutch authors; Van Gelderen (1948) and Verbiest (1950) have described a similar syndrome which they called "Ein Orthotisches (Lordotisches) Kaudasyndrom", and which has been named more recently "Dysbasia cum Dysstasia" by Steenwinkel (1959). Their patients differed from ours in that symptoms only developed on standing, whereas our patients obtained relief by standing still. Some of their patients could continue walking after developing sensory symptoms, and could produce enough motor weakness to make them fall down. These authors dismiss a vascular mechanism and emphasise, as the important pathological anomalies, a stenosis of the lumbar canal, stretching of the cauda equina nerve roots on standing up, and the lordosis of the lumbar spine disturbing the relationship of the emerging nerve-roots at the intervertebral foramina. They find difficulty, however, in explaining the absence of root pain on raising the intrathecal pressure when coughing, sneezing, or straining, in the presence of mechanical compression of the affected roots.

Vascular Factors

Interference with venous return alone seems unlikely to be important because of the generous venous anastomosis in the

spinal canal and the reversible venous flow round the nerve-roots (Gillilan 1958). Moreover the symptoms in some patients disappeared within half to one minute of ceasing to walk, which would seem to be too rapid to relieve venous stagnation in the upright position. A relevant observation is the unimpaired peripheral-nerve conduction when venous congestion is extreme after thrombosis of the main venous drainage of a limb.

A more likely explanation is provided by the findings of Blau and Rushworth (1958), who have shown an increased density and dilatation of the blood-vessels in the lumbar spinal cord of mice on the same side as an exercised hind limb which was made to work by electrical stimulation at two-second intervals for thirty minutes or longer. Of more importance to our present thesis is the observation of Blau and Rushworth that the vessels of the spinal nerve-roots were particularly prominent and often widely dilated in exercised animals.

We postulate that, when a person walks, there is a similar increased flow in the blood-vessels of the cauda-equina roots with an increase in size and possibly number of afferent and efferent blood-vessels. If this is true, then in those patients with firm constriction of the nerve-roots by the disc protrusion, the increased dilatation and increased blood-supply in response to activity of the roots is prevented by the compression, and symptoms of ischæmic neuritis result. This would accord well with the clinical observation of the constant amount of activity needed to produce the symptoms and its rapid resolution as soon as activity ceases, as well as with the physiological data of the evolution of sensory before motor symptoms in ischæmic nerve compression (Lewis et al. 1931).

Differential Diagnosis

One of the reasons for reporting this syndrome is its simulation of intermittent claudication arising from aortic or common-iliac-artery obstruction. It is not likely to be confused with peripheral arterial disease for the cramping pain, and the nutritional and colour changes in the legs, together with the absent pulses in arterial disease would clarify the diagnosis beyond doubt. When the arterial obstruction is situated more proximally, however, the problem of differentiation may be a real one and will be considered in detail.

Pain and Discomfort

In both conditions, patients may have painful symptoms related to exercise. In vascular disease this is usually " gripping ", whereas our patients complained of burning " pins-and-needles " or a painful numbness; and 1 had " knife-like ", but not gripping, pain.

Pain may, however, be absent in both diseases. 2 of our patients (cases 4 and 5) had numbness and pins-and-needles but no pain. A similar feature in aortic obstruction has, however, been stressed by many writers since Leriche's original description in 1923, which was summarised recently by Jeurgens (1958) who wrote: " It should be emphasized that the patient experiencing claudication from aortic obstruction will not always complain of pain. This distress has been described variously as: fatigue, weakness, incoordination, tightness, fullness, heaviness, cramp or tingling paresthesiæ " —a description which would well cover the symptoms in these cases of compression of the cauda equina.

Distribution of Pain and Paræsthesiæ

In vascular disease the common site of pain is the calf, but is often perceived in addition, or alternatively, in the thighs, buttocks, lower back, or even lower abdomen. The evolution of symptoms may be a helpful diagnostic point: in vascular disease, the symptoms commonly occur in the various sites simultaneously, whereas in this disc syndrome there is a definite march of sensations from area to area either centripetally or centrifugally, sometimes spreading up one leg and then down the other.

Peripheral Arterial Pulsation

The presence and extent of arterial pulsation would, at first sight, seem to be a crucial distinguishing feature. Yet it is by no means unequivocal, since both conditions occur in middle and old age, and a patient with a disc protrusion may well have poor arterial pulsation in the legs from concomitant mild but symptomless atherosclerosis as did 1 of our patients (case 1). On the other hand, reasonable preservation of the pulses is not uncommon in aortic insufficiency.

Neurological Signs

Muscle wasting and hypotonia may be present or absent in both conditions. In aortic disease it was noted in all 8 patients of Kekwick et al. (1952) and 12 out of 22 patients of De Bakey et al. (1954). Furthermore it was confined to one gluteal muscle group in 1 of the patients of de Wolfe et al. (1954); and since, in addition, the right ankle-jerk was diminished and S 1 anæsthesia was present, a myelogram, which proved to be normal, was done. One year elapsed before an aortogram established the diagnosis.

Sensory changes in vascular disease are exceptional but were absent in 2 of the cases reported here and were very slight in 3 others.

In aortic disease, the ankle-jerks may be reduced or absent; and in 2 of our patients were present or reduced.

Investigations

Lumbar puncture.—C.S.F. findings may be unhelpful in distinguishing vascular disease from this condition, particularly if the lesion is below the level of the L 3/4 disc, for spinal puncture in routine investigation is usually carried out at or above this level. A raised protein content, however, will suggest a spinal cause for the symptoms.

Radiological findings.—Calcification of the aorta is an unreliable diagnostic guide in vascular disease, as are plain radiographs of the lumbar spine in this disc syndrome.

In distinguishing between the two conditions the features more suggestive of the diagnosis of intermittent claudication of the cauda equina are these: (1) a paræsthetic quality of the discomfort; (2) a definite march of symptoms along the lower limbs; and (3) the presence of sensory change in the lumbar or sacral dermatomes.

In the individual case, however, the only unequivocal investigations are myelography and aortography, and both may have to be done to establish the diagnosis.

Another possible diagnosis is that of intermittent claudication of the spinal cord, in which Dejerine (1911) describes the symptoms as being " des crampes vagues . . . il n'y a pas de douleur à proprement parler . . . bien plus une sensation de poids et de raideur ". In these patients, however, examination shows positive evidence of an upper-motor-neurone lesion indicating that the origin lies in the spinal cord, although in the case he describes he attributes the lesion to lumbar ischæmia.

Summary

6 patients had pain or paræsthesiæ in the lower lumbar and sacral dermatomes after walking a definite distance. Symptoms related, at first intermittently and later quantitatively, to exercise were relieved within a half to three minutes by standing still. Persistent paræsthesiæ were sometimes present, but sciatic pain was absent. Physical signs ranged from reduced ankle-jerks to an obvious cauda-equina syndrome.

5 of the 6 cases were operated on, and in all an anterior disc protrusion with severe localised arachnoiditis was found. Decompression, with or without removal of the protruded disc, resulted in complete relief of the intermittent symptoms, although any pre-existing neurological deficit remained largely unaltered.

Lumbar spinal X-rays and cerebrospinal-fluid protein may be normal, but myelographic appearances of a " block " combined with thickened nerve-roots are diagnostic.

The differential diagnosis and presumed mechanism are discussed.

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REFERENCES

Blau, J. N., Rushworth, G. (1958) *Brain*, **81**, 354.
De Bakey, M. E., Creech, O., Cooley, D. A. (1954) *Ann. Surg.* **140**, 290.
de Wolfe, V. G., Lefevre, F. A., Humphries, A. W., Shaw, M. B., Phalen, G. S. (1954) *Circulation*, **9**, 1.
Dejerine, J. (1911) *Pr. Méd.* **19**, 981.
Denny-Brown, D., Brenner, C. (1944) *Arch. Neurol. Psychiat., Chicago*, **51**, 1.
Gillilan, L. A. (1958) *J. comp. Neurol.* **110**, 75.
Jeurgens, J. L. (1958) *Med. Clin. N. Amer.* **42**, 981.
Kekwick, A., Macdonald, L., Semple, R. (1952) *Quart. J. Med.* **21**, 185.
Leriche, R. (1923) *Bull. Soc. Chirurgiens Paris*, **49**, 1404.
Lewis, T., Pickering, G. W., Rothschild, P. (1931) *Heart*, **16**, 1.
Lewtas, N. A., Dimant, S. (1957) *J. Fac. Radiol., Lond.* **8**, 276.
Steenwinkel, F. L. M. (1959) *Ned. Tidjschr. Geneesk.* **103**, 2005.
Van Gelderen, C. (1948) *Acta psychiat. Kbh.* **23**, 57.
Verbiest, H. (1950) *Ned. Tidjschr. Geneesk.* **94**, 2415.

THE APLASTIC CRISIS IN SICKLE-CELL ANÆMIA

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With illustrations on plate

WHEN a patient with sickle-cell anæmia is followed for a long time, the hæmoglobin level (usually 7·0–8·5 g. per 100 ml.) and reticulocyte-count (usually 10–20%) are very constant. The balance between the accelerated rate of blood destruction and the greatly increased erythropoietic activity of the bone-marrow is precise. At the same time, episodes of severe anæmia are sometimes seen, more particularly in children, and investigation shows that the fall in red-cell count is usually due to temporary failure of erythrocyte production. As well as severe anæmia a reticulocytopenia is found and the degree of jaundice is often somewhat diminished. We have observed these "anæmic crises" in two groups of patients with sickle-cell anæmia:

The first group, usually under the age of two years, have an associated megaloblastic anæmia which responds specifically to folic acid with a return of hæmoglobin and reticulocyte levels to figures which may be regarded as normal for sickle-cell anæmia. Five examples of this syndrome have been reported in detail (MacIver and Went 1960).

The second group, usually older children, show either a severe erythroid hypoplasia of the bone-marrow, or a more or less complete maturation arrest at a primitive level.

Such aplastic crises were first recognised in hereditary spherocytosis (Owren 1948), but a similar mechanism is responsible for the acute anæmic episodes which may complicate the course of other chronic hæmolytic anæmias.

Gasser (1949), Davis et al. (1952), and Miesch et al. (1957) have reported cases associated with acquired hæmolytic anæmias. Larrain et al. (1950) and Crosby (1953) have reported aplastic crises in association with paroxysmal nocturnal hæmoglobinuria. Fessas (1959) states that aplastic crises with prolonged erythroblastic maturation arrest are common in thalassæmia major during intercurrent infections. Jandl and Greenberg (1959) describe three aplastic episodes, over a period of 3 years, in an adult with Cooley's anæmia of mild to moderate severity.

Only fourteen reports of an aplastic crisis in sickle-cell anæmia have been found.

Singer et al. (1950) observed an aplastic crisis during the course of virus pneumonia in a patient with sickle-cell anæmia. These workers mentioned a second case in a footnote. Chernoff and Josephson (1951) reported from the same institution four more cases which they had seen within a year. Diggs (1956) observed an aplastic crisis in a 16-year-old girl with sickle-cell anæmia. Leikin (1957) reported five cases in two families, and Miesch et al. (1957) reported another case in a 25-year-old negro. At the conference on hæmoglobin in 1957, Smith and Conley (1958) described an aplastic crisis in a 4-year-old boy.

Diggs' (1956) studies seem to confirm the rarity of this condition, since he observed only 1 aplastic crisis in a series of 747 clinical crises in a hundred and sixty-six patients with sickle-cell anæmia. But our impression is that aplastic crises in sickle-cell anæmia are much commoner than the literature would suggest, and in support of our contention we report here twelve cases, ten of which were seen over a period of less than 7 months. Seven of these cases were in three families. Although a familial incidence of aplastic crises in hereditary spherocytosis has long been recognised, only one previous report refers to sickle-cell anæmia (Leikin 1957).

Materials and Methods

The laboratory data on admission, together with short clinical summaries, are in table I, and the bone-marrow findings in table II. The laboratory methods have already been described in detail (MacIver and Went 1960).

Discussion

Mechanism of the Aplastic Crisis

Sickle-cell anæmia, like hereditary spherocytosis, is a chronic hæmolytic anæmia; the red cells are abnormal in shape and are destroyed prematurely by the reticulo-endothelial system. It has been shown (Callender et al. 1949) that the red-cell survival in this disease is 15–60 days, as compared with the normal 120 days. But the erythroid tissue of the bone-marrow has an enormous reserve capacity and under extreme stress is capable of increasing its output six to eight fold, which could theoretically compensate for a cell-survival time as low as 20 days (Crosby and Akeroyd 1952, Giblett et al. 1956). In sickle-cell anæmia this compensation is never quite complete, which explains the moderately severe anæmia usually seen in the disease.

It is well known that patients with sickle-cell anæmia have crises. The word crisis implies a sudden and striking change in the symptoms and signs of a disease, and the term was first used with reference to sickle-cell disease by Sydenstricker (1924). He pointed out that attacks of abdominal pain associated with an "... increase in jaundice and in the urobilin content of the urine ..." resembled closely the crises of hereditary spherocytosis. Since then the concept of hæmolytic crises in sickle-cell anæmia has been widely held. Singer et al. (1950) distinguished three types of crisis in sickle-cell anæmia: (1) the aplastic type, caused by a sudden cessation in the delivery of cells without any exaggeration of the already accelerated hæmolysis; (2) the hyperhæmolytic type, induced by an abrupt augmentation of erythrocyte destruction above the pre-crisis level without any primary interference with production and release; and (3) the aplastic-hyperhæmolytic type, a combination of absent

TABLE I—CLINICAL SUMMARY AND HÆMATOLOGICAL DATA OF APLASTIC CRISES ON ADMISSION

Case no.	Age (yr.)	Date seen	Length of history (days)	Summary of symptoms	Hb (g. per 100 ml.)	Reticulocyte count	Serum-bilirubin (mg. per 100 ml.)	
							Direct	Total
1	9	Nov. 23, 1956	5	Headache, pains in neck, fever	2·7	1·4	..	..
2	$6^{10}/_{12}$	Oct. 27, 1959	8	Umbilical pain, fever, vomiting, and pallor	1·8	0·1	0·3	2·0
3	$3^{11}/_{12}$	Dec. 16, 1959	5	Abdominal pain, fever	2·5	0·1	..	..
4 Family A	6	Jan. 6, 1960	7	Fever	2·8	1·4	0·2	1·3
5 Family A	11	Jan. 26, 1960	4	Abdominal pain, fever	2·0	0·2	..	..
6* Family A	34	Feb. 7, 1960	2	Pain in back and legs, headache	4·6	1·6	0·2	0·7
7 Family M	$5^{7}/_{12}$	March 28, 1960	11	Weakness, abdominal pain	2·8	0·3	0·6	2·0
8 Family M	15	March 20, 1960	9	Headache, fever	4·0	5·0	..	..
9	5	May 3, 1960	4	Fever, pain in epigastrium, low back, hip, and knees	2·1	0·1	0·1	0·6
10 Family B	6	May 16, 1960	6	Fever, headache, vomiting, and abdominal pain	2·7	0·1	0·4	0·4
11 Family B	7	May 17, 1960	8	Fever, headache, abdominal pain, and pallor	2·8	0·1	..	..
12	9	Sept. 6, 1960	4	Fever, pallor, vomiting, and pain in the back	4·0	0·1	..	..

* Case 6: this patient has sickle-cell hæmoglobin-C disease, and is the mother of cases 4 and 5.

delivery of cells associated with greatly increased hæmolysis. We have never observed a hyperhæmolytic crisis, and it seems probable that this type of crisis occurs rarely, if ever, in sickle-cell anæmia. This is also the view of Chernoff (1955) and Zuelzer (1959). Diggs (1956), who observed 747 clinical crises in a hundred and sixty-six patients with sickle-cell anæmia, found no evidence of more severe anæmia during or after the crisis and no significant or consistent alteration in the reticulocyte-count, bilirubin level, or urobilinogen excretion.

At the same time, cases of sickle-cell anæmia are sometimes seen with excessive splenomegaly and chronic anæmia of greater severity than usual for the disease. In such cases, where the spleen is overactive in destroying cells, splenectomy may be of benefit and transfusion requirements may thereby be diminished or cease altogether (Sprague and Paterson 1958). But there is no crisis of hyperhæmolysis in these cases; red-cell survival is continuously shortened even below the usual for sickle-cell anæmia, the condition being essentially chronic.

Basically, therefore, there are only two types of crisis in sickle-cell anæmia:

The clinical or painful crisis, due to erythrostasis of sickled red cells, resulting in infarction of various tissues. Characteristically, painful crises affect the bones or abdomen (Golding et al. 1959). Infarction of the spleen is almost invariable, and a wide variety of organs and tissues may be involved. Pulmonary infarction is also extremely common, and cerebral infarction may occur (Smith and Conley 1958).

The aplastic or hæmatological crisis.—In hæmolytic anæmia the balance between production and destruction of red cells is very delicately poised. If, as may be the case in sickle-cell anæmia, red-cell survival is as short as 15 days, it only requires erythrocyte production to be compromised for a relatively short time for the anæmia to increase strikingly.

TABLE II—BONE-MARROW FINDINGS: DIFFERENTIAL COUNT OF NUCLEATED RED-CELLS

Case no.	Myeloid/erythroid ratio	Proerythroblasts (%)	Normoblasts		
			Early (%)	Intermediate (%)	Late (%)
1	2/1	8·5	8·0	11·5	2·0
2	6·6/1	4·6	1·9	0·4	0·5
	6·4/1	4·7	0·9	0·7	0·3
	1·4/1	6·8	19·4	4·5	0·6
	1/2·2	1·0	10·2	37·4	14·2
	1/1·4	0·2	2·6	15·6	30·4
3	1/4	1·0	15·5	37·0	21·5
4	1/3·9	4·0	20·0	43·0	5·0
5	1/1·1	31·0	16·0	3·0	0
6	1/1·7	1·5	8·0	16·0	36·5
7	1/2·3	0·5	10·5	24·0	34·0
8	No bone-marrow examination				
9	18·5/1	1·0	0·8	0·8	1·0
	11/1	4·6	1·4	0·2	0·2
10	1/2·2	1·6	16·2	31·4	16·2
11	1/1·7	4·6	25·2	21·8	8·4
12	1/2·1	3·8	30·8	25·4	2·8

Singer et al. (1950) showed in their case that the hæmoglobin and red-cell count fell by about 50% in 3 days. Leikin (1957) also observed a drop of about 50% in two patients in 5–7 days. Singer et al. (1950) were able to show that, when the red cells of their patient, after recovery, were injected into another patient with sickle-cell anæmia, about 50% were eliminated in 3 days. After that the rate of destruction slowed down. From the shape of the red-cell-disappearance curve Singer et al. (1950) argued that the red-cell population in sickle-cell anæmia was not homogeneous, and later (Singer and Fisher 1952) they gave data suggesting that sickle hæmoglobin and fœtal hæmoglobin are not distributed uniformly throughout the red-cell population in this disease.

We have previously suggested (Went and MacIver 1958) that fœtal hæmoglobin may, by reason of its high solubility, exert a protective effect on the red cells against in-vivo sickling and consequent destruction by the spleen. If this is true then, in an aplastic crisis, the cells containing largely sickle hæmoglobin would be destroyed more rapidly than cells with slightly less sickle hæmoglobin and more fœtal hæmoglobin. In consequence some elevation of the fœtal hæmoglobin level might be expected at the height of the aplastic crisis as compared with the level before the crisis, or later during recovery. Our findings in three cases, which were not transfused, support this idea. In case 10 the levels were 7·3% on the 2nd day, and 4·0% on the 12th day. In case 11 they were 5·8% on the 3rd day and 2·6% on the 11th. In case 12 values of 10·3%, 10·5%, 9·0%, and 7·6% were found on the 3rd, 7th, 9th, and 14th days respectively.

We regard these differences as significant, and they support the view that the red-cell population in sickle-cell anæmia is not homogeneous, as a consequence of the non-uniform distribution of fœtal hæmoglobin in the red cells. The initial dramatic increase in anæmia in an aplastic crisis can be explained by postulating the rapid destruction of a highly susceptible group of red cells. Thereafter further anæmia develops more slowly, until spontaneous recovery follows because erythropoietic activity is resumed. The situation in hæmolytic anæmia contrasts strikingly with that in people with a normal red-cell survival (i.e., 120 days). That a hypoplasia or aplasia of erythroid tissue may also occur in such people has been shown by Gasser (1949) and Kölbl (1954). The development of anæmia, however, is then so gradual that it is likely to be missed unless specially sought, since a decrease in the red-cell count of the order of 1% a day is all that can be expected. Chernoff and Josephson (1951) describe a patient with an aplastic crisis associated with infectious mononucleosis, in whom the hæmoglobin level fell from 12·1 to 9·8 g. per 100 ml. in 13 days.

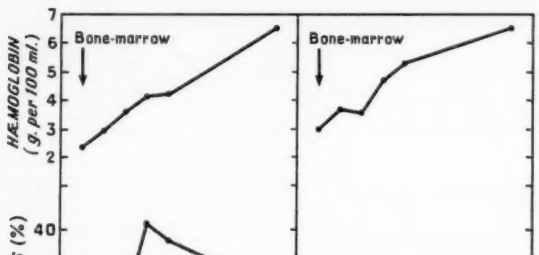

Fig. 3—Chart of hæmoglobin levels and reticulocyte-counts in cases 10 and 11, showing rapid spontaneous recovery from an aplastic crisis.

Clinical and Hæmatological Features of the Aplastic Crisis

The aplastic crisis often begins with a febrile illness associated with headache. There may be nausea and vomiting and often abdominal pain, but bone pain is rarely a striking feature in contrast to the painful crisis. The child shows increasing lethargy, and sometimes the mother notices pallor (cases 2, 11, and 12). In case 4 the mother said that the eyes had lost their usual yellow tinge with the onset of the crisis. Clinical examination usually reveals little apart from pallor, although there may be slight fever.

The blood-count shows a characteristic picture; anæmia is severe, sometimes below 2·0 g. Hb per 100 ml. of blood, and the reticulocyte-count is very low. Nucleated red cells are usually absent at this stage. Since spontaneous recovery is the rule the findings on bone-marrow biopsy depend upon the stage at which the examination is made (table II). In two cases (2 and 9) a striking hypoplasia of the erythroid tissue was found, the myeloid/erythroid ratios being 6·6/1 and 18·5/1 respectively. Plasma-cells were numerous in these cases. Singer et al. (1950) and Leikin (1957) also observed an increase in plasma-cells. In case 2, on admission, a few proerythroblasts could be seen (fig. 1), but more mature erythroid cells were very scanty. Daily bone-marrow examinations were made on this patient, and it was possible to follow the progress of recovery. By the 3rd day an erythroid hypoplasia had become an erythroid hyperplasia, with a myeloid/erythroid ratio of 1·4/1, but most cells were still at the early normoblast stage. On the 4th day intermediate normoblasts were numerous, but next day late normoblasts preponderated. A reticulocytosis in the peripheral blood followed. In the remaining cases recovery had already begun when the bone-marrow was examined so that erythroid hyperplasia with various degrees of maturation arrest was seen. Usually the predominant cell types were proerythroblasts and early normoblasts (fig. 2), although in some cases numerous intermediate and even late normoblasts were present. But the low reticulocyte-count in the peripheral blood of these cases indicated that delivery of red cells in any quantity had not yet begun.

During the recovery period a characteristic finding was the sudden appearance of large numbers of nucleated red cells in the peripheral blood. In cases 7, 9, 10, 11, and 12 the normoblasts numbered 68,400, 74,100, 136,000, 108,000, and 131,000 per c.mm. respectively. This outpouring of normoblasts preceded the appearance of reticulocytes by a day or so, and persisted for some days afterwards.

It is not rare to find large numbers of nucleated red cells in the peripheral blood, together with a high reticulocytosis and a hyperplastic bone-marrow, in patients with sickle-cell anæmia, who have been admitted to hospital because of a "crisis". Diggs (1956) comments that the hæmatological course in these patients is characterised by a gradual return towards normal in erythrocyte values, without significant change in the concentration of serum-bilirubin: "It is probable that such persons were in the recovery phase, following an aplastic or hypoplastic crisis." We agree with this, and suggest further that aplastic crises are probably quite common, but because of the mildness of the symptoms and the self-limiting nature of the bone-marrow failure most of these cases may never be seen in hospital. We are firmly convinced that aplastic crises and painful crises are entirely distinct. Pain is not usually a striking feature in the aplastic crisis, though on the other hand a severe painful crisis can arise, even resulting in death, without any fall in the hæmoglobin level.

Those cases which were not transfused developed spontaneously a high reticulocytosis and the hæmoglobin level returned rapidly to a figure which may be regarded as normal for the disease (fig. 3). In contrast a much smaller reticulocytosis was seen in patients treated by blood-transfusion. Blood-transfusion is known to inhibit erythropoiesis temporarily, and in our view it can usually be avoided safely in cases where bone-marrow examination shows that recovery from the aplastic crisis is well advanced.

Ætiology of the Aplastic Crisis

The mechanism whereby the severity of the anæmia in a hæmolytic anæmia may increase rapidly due to temporary failure of erythropoiesis has already been discussed. The immediate cause of this failure is not certain. In hereditary spherocytosis it seems likely that extrinsic, perhaps infective, factors are responsible. Evidence for this is the well-known occurrence of crises either simultaneously or in rapid succession in several members of the same family, the signs of an upper respiratory infection often being associated. Horne et al. (1945) placed a ferret in the home of an affected family and it soon died, apparently of influenza.

With regard to sickle-cell anæmia, the patient reported by Singer et al. (1950) had a typical virus pneumonia associated with his aplastic crisis, and his sister, who also had sickle-cell anæmia, was admitted to another hospital on the same day with

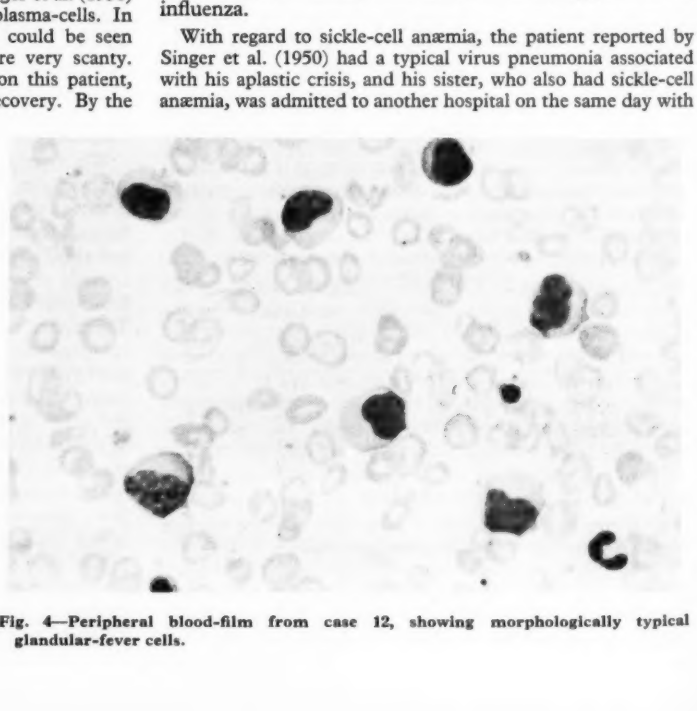

Fig. 4—Peripheral blood-film from case 12, showing morphologically typical glandular-fever cells.

similar complaints but apparently without an aplastic crisis. From the data given, however, it seems quite likely that the sister was already in the recovery stage.

Of the four patients reported by Chernoff and Josephson (1951), one had an aplastic crisis in association with a *Salmonella choleræsuis* septicæmia, whereas in the others the crisis seemed to be related to vague upper-respiratory infections. In the case described by Diggs (1956) the onset was associated with an unexplained fever. Leikin (1957) reported two families in each of which two siblings had an aplastic crisis. A third member of one family was undoubtedly in the recovery stage at the time of admission. The onset of the crises in these families appeared within a 2-week period in each set of patients. Signs of infection were not remarkable, one patient in each family having mild pharyngitis and tonsillitis, and one patient in the other family having an upper-respiratory-tract infection. The moderate numbers of monocytes and plasma-cells in the peripheral blood of four of these cases was thought to suggest infection, but extensive bacteriological and viral studies proved unrewarding. The patient reported by Miesch et al. (1957) had had a " cold " for 3 or 4 days before the onset of the crisis, but the case of Smith and Conley (1958) had a crisis in the absence of fever or pain.

In our cases more than one member of a family was affected in three instances. In one family (cases 4, 5, and 6) two children became sick 20 days apart, and the mother, with sickle-cell hæmoglobin-C disease, was smitten 15 days later. In another family (cases 7 and 8) two sisters were affected, although the second was not investigated sufficiently to prove the diagnosis beyond all doubt. In the third family (cases 10 and 11) a brother and sister were admitted to hospital on successive days. Antecedent symptoms suggesting infection were present in most cases of this series. There was a history of fever in ten cases, of headache in five, and of abdominal pain in seven. These symptoms were acute in onset, preceding admission by 2–11 days. Despite extensive bacteriological investigation, including cultures of blood, stool, and urine, no pathogens could be incriminated. Virus studies likewise failed to produce any definite evidence of recent infection although complement-fixing antibodies were found in some cases to mumps, influenza A, adenovirus, coxsackie B, and Q fever—indicating infection at some undetermined time.

In case 12 large numbers of atypical mononuclear cells appeared in the peripheral blood during the period of recovery from the aplastic crisis, and these were morphologically typical of glandular-fever cells (fig. 4). Heterophile antibodies were found in the serum on four occasions at a titre of 1/28. One case, without sickle-cell anæmia, has been reported to have erythroid aplasia associated with infectious mononucleosis (Chernoff and Josephson 1951).

Several different factors may probably be associated with an acute failure of erythropoiesis. Gasser (1949) described a series of ten cases in which all but two had no antecedent hæmatological disorder. One was associated with an atypical pneumonia, one with diphtheria, two with allergic reactions to drugs (phenobarbitone and oil of chenopodium), three with anaphylactoid purpura, and one with erythroblastosis fœtalis. Kölbl (1954) also described a case associated with an anaphylactoid syndrome (subsepsis allergica). These observations suggest that failure of erythropoiesis may result from toxic or allergic factors as well as infective agents.

Summary

Of 12 patients with an aplastic crisis associated with sickle-cell disease, eleven were children with sickle-cell anæmia, and one was an adult with sickle-cell hæmoglobin-C disease.

Ten of the cases were seen over a period of less than 7 months, and the syndrome may be commoner than has previously been supposed.

Evidence is given to support the hypothesis that the distribution of sickle and fœtal hæmoglobins in the erythrocytes in sickle-cell anæmia is not homogeneous.

The fact that seven of the cases belonged to three families implies that infection may play an important ætiological role. This view is supported by the clinical presentation, and by the fact that one patient apparently had infectious mononucleosis. Bacterial and viral studies failed to demonstrate any ætiological agent in these cases.

We are very grateful to Dr. E. H. Back for allowing us to study these patients, and to Dr. Louis Grant and Dr. M. Sigel for extensive bacteriological and viral studies. This work was supported in part by a grant from the Colonial Office at the instance of the Colonial Medical Research Committee. E. J. P.-W. is in receipt of a Colonial Research fellowship.

REFERENCES

Callender, S. T. E., Nickel, J. F., Moore, C. V., Powell, E. O. (1949) *J. Lab. clin. Med.* **34**, 90.
Chernoff, A. I. (1955) *New Engl. J. Med.* **253**, 365.
— Josephson, A. M. (1951) *Amer. J. Dis. Child.* **82**, 310.
Crosby, W. H. (1953) *Ann. intern. Med.* **39**, 1107.
— Ackeroyd, J. H. (1952) *Amer. J. Med.* **13**, 273.
Davis, L. J., Kennedy, A. C., Baikie, A. G., Brown, A. (1952) *Glasg. med. J.* **33**, 263.
Diggs, L. W. (1956) *Amer. J. clin. Path.* **26**, 1109.
Fessas, P. (1959) *in* Abnormal Hæmoglobins (edited by J. H. P. Jonxis and J. F. Delafresnaye); p. 134. Oxford.
Gasser, C. (1949) *Helv. pædiat. acta*, **4**, 107.
Giblett, E. R., Coleman, D. H., Pirzio-Biroli, G., Donahue, D. M., Motulsky, A. G., Finch, C. A. (1956) *Blood*, **11**, 291.
Golding, J. S. R., MacIver, J. E., Went, L. N. (1959) *J. Bone Jt Surg.* **41B**, 711.
Horne, J. L., Lederer, H., Kirkpatrick, H. J. R., Leys, D. G. (1945) *Lancet*, ii, 33.
Jandl, J. H., Greenberg, M. S. (1959) *New Engl. J. Med.* **260**, 461.
Kölbl, H. (1954) *Z. Kinderheilk.* **75**, 525.
Larrain, C., Del Solar, A., Maccioni, A., Perez, A. (1950) *Rev. med. Chile*, **78**, 735.
Leikin, S. L. (1957) *Amer. J. Dis. Child.* **93**, 128.
MacIver, J. E., Went, L. N. (1960) *Brit. med. J.* i, 775.
Miesch, D. C., Baxter, R., Levin, W. C. (1957) *Arch. intern. Med.* **99**, 461.
Owren, P. A. (1948) *Blood*, **3**, 231.
Singer, K., Fisher, B. (1952) *ibid.* **7**, 1216.
— Motulsky, A. G., Wile, S. A. (1950) *J. Lab. clin. Med.* **35**, 721.
Smith, E. W., Conley, C. L. (1958) *in* Conference on Hemoglobin; p. 276. Publication 557, National Academy of Sciences. Washington, D.C.
Sprague, C. C., Paterson, J. C. S. (1958) *Blood*, **13**, 569.
Sydenstricker, V. P. (1924) *Trans. Dis. Child. Amer. med. Ass.* p. 77.
Went, L. N., MacIver, J. E. (1958) *Blood*, **13**, 559.
Zuelzer, W. W. (1959) *in* Abnormal Hæmoglobins (edited by J. H. P. Jonxis and J. F. Delafresnaye); p. 100. Oxford.

STANNOSIS

Benign Pneumoconiosis due to Tin Dioxide

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With illustrations on plate

IN 1955 an account was given of some radiographic chest abnormalities which were thought to be due to the inhalation of tin-oxide dust or fume (Robertson and Whitaker 1955). There were 121 patients in whom these changes were found, and they were probably the first

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examples in this country of a rare condition, of which only 13 cases had previously been reported. Although the diagnosis of a benign pneumoconiosis due to tin oxide seemed reasonably certain, there was no confirmation at that time. These patients had no symptoms or signs referable to their lungs, but most peculiar densities were seen in their chest radiographs. It has not been easy to acquire lung tissue: over the past five years, only a few of our original 121 patients have died, but almost all of them have been studied. We have obtained the lungs from 7 of these workers in the tin-smelting industry, and we report our findings after pathological examination, chemical and X-ray-diffraction analysis, and X-ray-emission spectroscopy.

The Process

Tin is smelted in Liverpool from cassiterite (mainly tin dioxide) brought from Bolivia and Nigeria in a concentrated form. It comes in bags which have to be opened and emptied into " skips " during which time a sample is taken for analysis so that a proper price may be agreed between the mine owner and the tin smelter. The ore is next taken to a calcine furnace along a conveyor belt without much dust at either end; it used to be " trammed " in small bogies, and old hands in this ore-haulage department say that the conditions then were very dusty. In the calcine furnace, the ore is roasted to burn off some impurities, washed with water, and mixed with anthracite duff. When it is reduced and smelted hot gases (thought to be tin dioxide) arise from the molten metal as it leaves the furnace (fig. 1). There have been many changes in the working conditions over the years which would affect the amount of dust to which the workers were exposed. A film, made in 1954 to illustrate this process, has been described (Robertson 1960); but full details, including a dust survey, will be published later.

Case-records and Clinical Features

Patient 1 joined the company in 1901, aged 26. He retired at 73, after forty-six years' work at the furnaces, where he inhaled tin fume for roughly an hour a day. At 78, he had no symptoms, could run upstairs, and claimed that he had never lost any time with a chest illness (figs. 2 and 3). He died in 1957, aged 82, probably from cerebral thrombosis: a full necropsy was not performed.

Patient 2 joined the company in 1923, aged 16. He worked as a furnace charger for thirty-three years, using various methods—at first manual and later mechanical. There were hazards from one particular process on top of a now disused blast furnace, and also from furnace tapping. In 1933 he had arsine poisoning, but never lost any time with chest illness, and claimed he felt better at work than when on holiday. He had a slight wheeze and seemed to have some bronchitis. He died in 1959, aged 52, from coronary thrombosis.

Patient 3 joined the company in 1919, aged 25. He worked in the calcine shed for thirty-eight years, during which time the hot (but not very dusty) calcined ore was dealt with by varying processes. When he was 60, he could run upstairs and ride a bicycle; he estimated that he walked seven miles a day, mostly up and down ladders. Radiographs showed an aortic aneurysm of moderate size. He died in 1958, aged 64, from coronary thrombosis.

Patient 4 joined the company in 1918, aged 33. He worked on the " skips " for twenty-nine years, retiring at 65; and at 69 he had no symptoms. This work is usually dusty, but he dealt more with the " cleaner " Nigerian ore. He died in 1959, aged 75, from cerebral thrombosis; he had had auricular fibrillation and an old myocardial infarction.

Patient 5 joined the company in 1923, aged 27. With the exception of three years, he worked entirely at the furnaces, spending fourteen years at the refinery and fourteen at the main smelting furnace. He played football until he was 56; and died in 1955, aged 59, from carcinoma of the stomach.

Patient 6 joined the company in 1919, aged 25. He worked entirely in the furnace department, spending four years at the refinery and twenty-nine at the smelting furnace. When he was 60, he could climb stairs comfortably, and he had never lost any time with chest illness. He died in 1959, aged 65, from bacterial endocarditis and uræmia.

Patient 7 joined the company in 1947, aged 40, and worked there for eleven years, mainly dealing with ore haulage and with smelting and slag charges. He died in 1959, aged 52, from coal-gas poisoning. His lungs were analysed; but, since some time elapsed before he was found, the histological appearances were not studied.

These patients had been examined by one of us at various times between 1953 and their death. There was radiological evidence of a pneumoconiosis in all (with the possible exception of patient 7), and the appearances of the films varied with the length and nature of the dust hazard. When this was largely tin-dioxide fume, there was a nodular appearance with opacities, each about 3–5 mm. in size. The early films showed fewer less opaque diffusely scattered larger nodules, and other features that have already been described in detail (Robertson and Whitaker 1955). In the furnaceman who had worked for over forty years at the same sort of job (patient 1), the opacities were denser and smaller. They were numerous and evenly distributed throughout all five lobes (fig. 2), with the " hard " mottling reaching the periphery of the lung fields, as is shown in a portion of the right upper lobe (fig. 3). In the original film lines of the pleural reflection around the mediastinum and on the diaphragm were just visible.

All the films were seen by four experienced readers from the Medical Research Council's Pneumoconiosis Research Unit at Penarth, and were put into categories $^1/_2$, 1, 2, or 3.

In this grouping, 1, 2, and 3 correspond to the classification for simple pneumoconiosis recommended by the International Labour Organisation at their conference on pneumoconiosis at Sydney in 1950 (Cochrane et al. 1951); $^1/_2$ was an early abnormality where there was evidence consistent with tin-dioxide deposition (e.g., the mediastinal pleural markings which are not seen in coalworkers). A new category of 4 to cover the extensive and dense opacities sometimes seen might have been used, and then patient 1 would just have come into this category. In table II, the summation of the four readings has been given; no two readers varied by more than one category in their assessments, nor did they find significant differences between the right and left lung fields.

Dr. J. C. Gilson and his colleagues from the Pneumoconiosis Research Unit have investigated almost all the employees at this works, and two tests of pulmonary ventilation (forced expiratory volume and airway resistance) showed no average decline in function with rising radiological category (Gilson 1960). They examined six of our patients (all except no. 7) and results of two of their lung-function tests are given in table II. Patient 2 had clinical bronchitis and emphysema, and coronary-artery disease from which he later died.

Pathological Features

Method

At necropsy, the lungs were inflated with formol saline; the better inflated one was retained for preparation of a whole-lung

TABLE I—PROCESSES AND HAZARDS IN A TIN-SMELTING WORKS

Process		Hazard
Tin-ore concentrate in bags		
↓		
Ore-receiving room		
↓		
Skips	——→	Dust+++
↓		
Calcine furnace		
↓		
Smelting furnace	——→	Tin-dioxide vapour++
↓		
Refinery furnace	——→	Dusty after-stuff+
↓		
Cast in bars		

section (Gough and Wentworth 1949), histological studies, and X-ray-emission microanalysis. The other was dried and used for dust identification by chemical and X-ray-diffraction analysis, and by electron microscopy.

Blocks typical of each whole lung were selected for the preparation of serial histological sections, which were stained with hæmatoxylin and eosin, with a silver-impregnation technique for reticulin, and by the Weigert and van Gieson method for collagen. The last section of the series was microincinerated at 550° to 600°C by the method of Irwin (1934).

The presence and degree of focal and general emphysema in sagittal lung sections (as judged by the gross appearances), and the amount of reticulin and collagen in the dust foci in the histological sections were graded as has been done in coal-workers' lungs (Rivers et al. 1960).

Macroscopic Appearances

Black or dark grey dust foci, 2 to 5 mm. in size, were distributed uniformly throughout the lung (fig. 4). No silicotic or fibrous nodules were seen. There was dust pigmentation of the interlobular septa, particularly where these projected into the lung from the pleura. This feature was present in all our tinworkers' lungs: it is common in simple pneumoconiosis of coalworkers, whose lungs look very similar to the naked eye.

Microscopic Appearances

The essential histological appearances were the same in all the lungs.

Dust.—The dust foci consisted of dense aggregates of dust-laden macrophages surrounding the respiratory bronchioles, though sometimes the dust deposition was more extensive and surrounded the entire length of the terminal non-respiratory bronchiole (fig. 5). Sometimes a few dust-laden cells were seen lying free in the alveoli (fig. 6); they were also seen in the lymphatics of the interlobular septa, and small numbers were in the pleura and in the perivascular lymphatics of vessels adjacent to the bronchioles. No extracellular dust was seen nor was there any dilatation of lymphatics. These findings resembled those seen when cassiterite of respirable size was insufflated into rats' lungs (Robertson 1960).

The focal emphysema seen in association with dust foci in coalworkers' lungs, was not a prominent feature in these tin-workers. Although dilatation of the respiratory bronchioles was seen microscopically, it was insufficient to produce more than very early focal emphysema (grade 1, as judged by the naked eye) in patient 1, who at 82, was our oldest subject and whose lungs contained the greatest amount of dust.

Little of the dust was burned away with microincineration alone (fig. 7), but when the sections were subsequently treated with concentrated hydrochloric acid, the dust disappeared. These findings are summarised in table II, where the patients are arranged in descending order of estimated total quantities of tin dioxide in one lung.

Dust Analysis

Chemical and X-ray Diffraction

Samples of dried ground tissue were ashed at 450°C, and total silica was determined chemically on a part of the ash. Another part of the ash was extracted three times with hot 10% nitric acid, and the residue, mainly tin dioxide and other acid-insoluble dust (residue A), was washed, dried, ashed at 450°C, and weighed. Part of this residue A was mixed with a large excess of ammonium iodide and heated at 450°C in order to volatilise the tin as SnI_4: the remainder of it was used for a study of the dust by X-ray diffraction and electron microscopy. After cooling, the remaining material was evaporated with concentrated nitric acid and reweighed (residue B), and the difference between the weights of residues A and B was taken to be tin dioxide. The amount of quartz was estimated visually from X-ray-diffraction patterns of residue B.

TABLE III—TIN-DIOXIDE CONTENT OF LUNGS

Patient no.	1	2	3	4	5	6	7
% Dried lung							
Residue A	4·8	2·9	2·9	3·8	1·9	1·4	0·8
SnO_2	3·9	2·6	2·0	2·1	1·6	0·8	0·6
SiO_2	0·3	0·08	0·3	0·8	0·1	0·1	0·04
Quartz	0·03	0·01	0·2	0·2	0·03	0·01	Nil
Grammes per lung (estimated)							
SnO_2	3·3	2·9	1·5	1·4	1·3	0·8	0·5
Quartz	0·02	0·01	0·15	0·2	0·02	0·01	Nil

Tests with a few milligrammes of tin dioxide and quartz of 1 μ average size, alone and in mixture, showed 100% loss for SnO_2 and 97% recovery for quartz by this method. The analytical results expressed as per cent. dried lung tissue were multiplied by the known or estimated lung weights to obtain the amount in grammes of tin dioxide per lung. Any uncertainty about the tissue weights will give a corresponding uncertainty in the amount of SnO_2 in grammes per lung; errors from this cause are not likely to exceed 0·1 g. SnO_2 in any of the seven lungs. The results are given in table III. The amount of tin dioxide varied from 0·5 g. to 3·3 g. per lung, and, in each case, it was additionally identified from its X-ray-diffraction spectrum, of which one example is shown in fig. 11, with the spectrum of SnO_2 given for comparison.

Typical electron micrographs of residue A are shown in fig. 8. The lung dust occurs in single particles or aggregates of particles of about 0·1 to 0·5 μ, which look very similar to

TABLE II—LUNG CHANGES IN STANNOSIS

Patient no.	Age at death	Years of service	Occupation	Radiographic category (summation of four observers)	V.C. (ml.)	I.M.V.V.* (litres per minute)	Estimated tin (g. per lung)	Emphysema (possible grades 0, 1, 2, 3)		Reticulin grade (0, 1, 2, 3)	Collagen grade (0, +, ++, +++, ++++)
								Focal	General		
1	82	47	Smelting furnace	12	2600	56	3·3	1	1	1	++
2	52	35	Smelting furnace	12	2300	32	2·9	0	1	0	0
3	64	39	Calcine shed	3	3200	90	1·5	0	0	1	+
4	75	32	Skips	12	2300	67	1·4	0	0	2	++
5	59	32	Refinery/smelting furnace	8	3000†	..	1·3	0	0	1	+
6	65	40 (30 in furnace)	Smelting furnace	5	3500	93	0·8	0	1	0	0
7	52	11	Ore haulage	½	4400	98	0·5	Histological findings not available			

* Indirect maximum voluntary ventilation = F.E.V.$_{0\cdot5}$ × 40. F.E.V. = forced expiratory volume. † Measured by a different observer. V.C. = vital capacity.

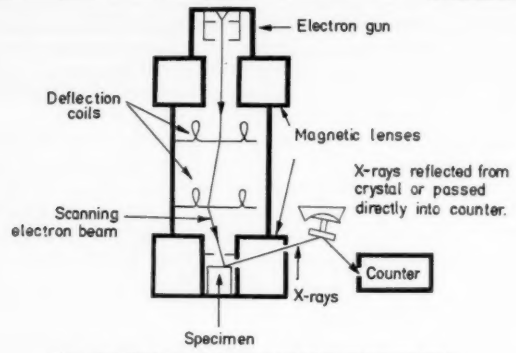

Fig. 12—Diagram of X-ray-emission microanalysis.

furnace fume collected at the taphole by a thermal precipitator (fig. 9).

X-ray-emission Microanalysis

Although we knew from the chemical analysis that these lungs contained tin dioxide, we had no proof for some years that the tin was, in fact, in the dust particles within the phagocytes. The identification of small particles in lung sections has now been achieved by X-ray-emission microanalysis. A beam of electrons, accelerated to 20–30 kV, is focused by two magnetic lenses into a small spot, or electron probe, 1 μ in diameter. This is directed on the unknown particle, which can also be as small a 1 μ, and the spectrum of emitted X rays plotted with a crystal spectrometer (fig. 12). The presence of any element in the periodic table can be recognised by the characteristic X-ray wavelength it emits, and its concentration deduced from the intensity of the emission. The lower the element in the periodic table, the longer is this characteristic wavelength, and for elements below about magnesium (atomic number 12) the wavelengths are so long that they cannot, at present, be readily detected.

An extension of the method, developed under Dr. V. E. Cosslett at the Cavendish Laboratory, Cambridge (Cosslett and Duncumb 1956, Duncumb 1959) uses a scanning technique to form an image of the specimen by its X-ray emission. The electron probe is scanned over the specimen, line by line, to cover an area of up to a half millimetre square on the surface. The emitted X rays are detected by a counter which varies the brightness of a cathoderay-tube spot scanning in synchronism with this probe. In this way, by representing the variation of X-ray emission over the surface, a magnified image of the specimen is built up on the screen. From this image, the electron probe can be accurately positioned on a selected point in the specimen and the characteristic spectrum plotted to give an analysis of the element present. Alternatively, the spectrometer can be used to select a particular emission wavelength, so that the scanning image shows up the distribution over the surface of the specimen of only the element emitting that wavelength.

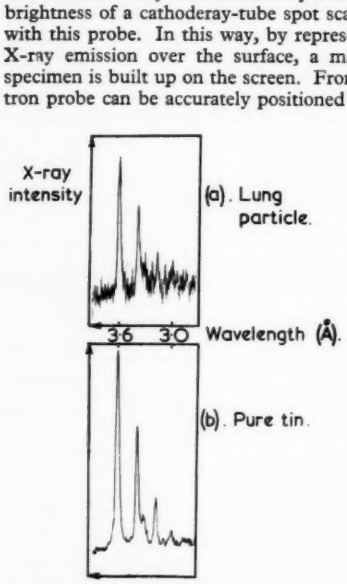

Fig. 13—X-ray-emission spectrum: (a) lung particle and (b) pure tin.

These techniques have been applied to a specimen of untreated dried lung from patient 5, and were later confirmed by investigations in one other patient (no. 1). A section through one of the dust foci was found to contain some dense particles, suspected from other evidence to be tin dioxide. The probe was positioned on a particle about 2 μ in diameter in the middle of the field, and the spectrum plotted (fig. 13a). Comparison with the spectrum from a piece of pure tin (fig. 13b) shows accurate correspondence in the characteristic emission wavelengths, and thus proves that the particle does in fact contain tin. Similar results were obtained with several other particles, and no tin was found in a section away from one of these dust foci. Oxygen (atomic number 8) radiates a wavelength too long to be detected, so that it was not possible to confirm by this method that the tin was present as the dioxide. In all cases, however, the dioxide has been identified by the X-ray-diffraction technique.

Discussion

When we first described the condition in this country, only 13 patients had previously been reported in the world's literature. The first was from Germany (Beintker 1944); there were 7 from Czechoslovakia (Bartak et al. 1948); and 5 others were from the United States (Pendergrass and Pryde 1948, Cutter et al. 1949, Dundon and Hughes 1950, Spencer and Wycoff 1954). Since then 10 patients have been reported from Chile (Schuler et al. 1958), and some environmental and experimental studies have been made (Oyanguren et al. 1958). Some examples have been found in Malaya (Scott and Picken 1960), but no necropsies have been made there.

It seemed obvious that if the men who empty bags of ore concentrate get a pneumoconiosis, so should the men who fill them. To test this, one of us (A. J. R.) has just visited the tin mines and the concentrating plants in Bolivia. Those who mine the ore have a great exposure to free silica dust, with resulting silicosis. In the plants, however, the silica particles of small size are washed out and the concentrate of cassiterite is put into bags and sent to Liverpool. 10 Bolivians with stannosis acquired during the bagging were discovered during this tour, and their radiographic appearances and clinical findings were identical with the workers in Liverpool: a full account of these patients will be published later. Although this now makes 33 cases, in addition to the 121 we have already recorded, we are aware of only 2 previous necropsy reports where pneumoconiosis due to tin dioxide—"stannosis"—was suspected (Bartak et al. 1948, Dundon and Hughes 1950).

The histological appearances are comparable with those reported by Dundon and Hughes (1950) in their excellent paper, though we did not observe any dilatation of lymphatics, and we see no reason to postulate that the dust causes lymphatic blockage. Lymphatic dilatation in their one case might have been caused by metastatic deposits from a prostatic carcinoma. 2 of our patients showed pathological evidence of bronchitis, but the others showed no signs of irritation of the bronchial epithelium or hypertrophy of mucous glands; nor did they show any other features thought characteristic of chronic bronchitis (Reid 1960).

We think that focal emphysema may best be related to both the amount of dust in the lung and the maturity of the dust foci. Although the smooth muscle of the bronchiole appears intact, its function may be progressively embarrassed by the cuff of dust-laden macrophages and the network of reticulin. The relatively increased reticulinosis and collagenisation of coal-dust foci would account for the higher grades of focal emphysema among coalworkers when compared with our tinworkers. Table II shows the remarkably low reticulin response to dust-laden macrophages, as well as the slight amount of collagen in

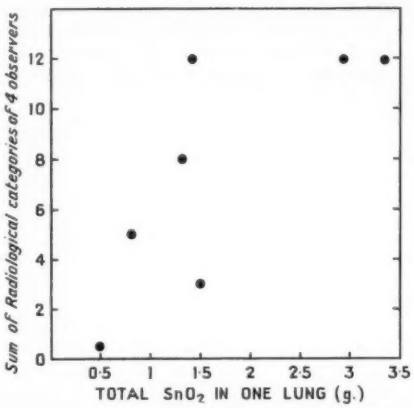

Fig. 14—Comparison of radiological category and total tin dioxide in one lung.

the dust foci. It may be that the collagen grade is related to the total time the dust has been present in the lung—over 50 years for some of the dust in patient 1. This long retention, seemingly without any ill-effect, is in sharp contrast to the toxicity of the organic dialkyl and trialkyl tin compounds (Barnes and Stoner 1958). Figures for normal indirect maximum voluntary ventilation at the age of over 80 are not readily obtained, but the level of 56 litres per minute in the patient of 82 with the most dust and the most advanced radiological change, appears to be as expected (estimated 55 litres per minute).

Bartak et al. reported the percentage of tin dioxide in the ashed lungs of their patient as 20·4%. Dundon and Hughes gave 13·4% tin dioxide in their patient's lung ash. Portions of lung from our patients 1 and 5 were analysed after ashing at 900°C and were found to contain 40% and 35% respectively of tin dioxide. We have not thought it useful to express our results in this way, but have estimated the actual amount of tin dioxide in one lung, with values ranging from 0·5 to over 3 g.: this figure is not affected by such variables as the weight of lung at death. Dundon and Hughes (1950) suggest that " it is likely that exposure to furnace fumes rather than dust from the finished product is the most important source of stannic-oxide pneumoconiosis ". It is difficult to imagine much dust arising from bars of tin; furnace fumes are just one source of tin dioxide, and we have already reported more patients with advanced pneumoconiosis among workers handling a dusty tin-ore concentrate in the ore-receiving house than among furnace workers. There is no need for any controversy over the " cause " of stannosis, since it is obvious that exposure of the patient to tin dioxide of respirable size in sufficient quantity will give the diagnostic radiographic appearances, whether the source be " fume " or " dust ".

There is a fairly good relation between the quantity of tin dioxide estimated in the lung and the radiological category (fig. 14). For comparable categories, the lungs of tinworkers appear to contain about one-tenth the amount of dust found in coalworkers with simple pneumoconiosis, although of course the higher atomic number of tin (50) makes it seen more readily than carbon (atomic number 6). An X-ray photomicrograph of a 1 mm.-thick section of lung (fig. 10) illustrates this point and clearly shows the distribution of radio-opaque material.

Dust in the lung phagocytes looks very like carbon dust found in the lungs of city dwellers or coalminers, and could easily be mistaken for it unless analysed. If it were carbon, it would disappear on microincineration, but it remains virtually unaltered, as fig. 7 shows. The dust-filled phagocytes are perhaps 15–30 μ in diameter, and since our electron probe can be positioned on a particle of 1–2 μ, the dust can be identified readily by this new method. We believe this is the first time that dust analysis within a phagocyte has been done in this way.

When the chest radiographs were first seen, silicosis had been suggested as a possible diagnosis. There never had been any clinical evidence of this, and now we know there is no pathological evidence of it, since the quantities (0–200 mg.) of quartz found in the lung are very small compared with the amounts (2–4 g.) found in classical silicosis. No examples of progressive massive fibrosis have been seen, and in none of our patients was the dust related to the cause of death.

The striking radiological changes, the good pulmonary function, the longevity of the workmen as a whole, and the absence of any significant pathological response to the tin dust in phagocytes, would seem to justify the title " *benign* pneumoconiosis due to tin dioxide " as an alternative to " stannosis ".

Summary

Clinical, radiological, and pathological findings are given for 7 workers from a tin-smelting works who had abnormal chest radiographs. They had no significant pulmonary fibrosis and no evidence of silicosis.

Chemical and X-ray-diffraction analysis showed that the lungs contained tin dioxide.

X-ray-emission microanalysis identified tin in a minute particle of dust in a lung phagocyte.

We have confirmed the diagnoses, made six years ago, of benign pneumoconiosis due to tin oxide.

We have always had the greatest cooperation from Mr. R. W. Scarlett, manager of the tin-smelting works, and from the Bootle Coroner and his officer (Serjeant Murphy). Dr. A. H. Cruikshank, Dr. D. A. Stanley, and Dr. M. J. J. Wodzinski obtained and inflated lungs; and the lungs from patient 2 were made available through the courtesy of Dr. G. B. Murray of the Manchester Pneumoconiosis Medical Panel.

Miss Rosalie Frye produced the X-ray photomicrograph, Mr. J. Skidmore made the thermal precipitator sample, Mr. J. Cartwright took the electron micrograph, and Mr. C. Casswell the X-ray-diffraction spectra. Mr. T. H. Cook and Mr. S. Gaunt took some photomicrographs; the rest of the photography was done by Mr. Wilfred Lee, F.R.P.S., and Mr. Eric Norman; and the paper section was obtained through the courtesy of Prof. J. Gough. Prof. E. J. King helped to organise our collaboration, and we must thank Prof. C. V. Harrison for his detailed and helpful criticism of our text.

Not only did Dr. J. C. Gilson and his colleagues from the Pneumoconiosis Research Unit visit the works and do lung-function tests, but they have continually given every possible help and encouragement with what has been a long investigation extending over six years.

REFERENCES

Barnes, J. M., Stoner, H. B. (1958) *Brit. J. industr. Med.* **15**, 15.
Bartak, F., Tomecka, M., Tomicek, O. (1948) *Cas. Lék. čes.* **87**, 915.
Beintker, E. (1944) *Reichsarbeitsblatt*, **3**, 37.
Cochrane, A. L., Davies, I., Fletcher, C. M. (1951) *Brit. J. industr. Med.* **8**, 244.
Cosslett, V. E., Duncumb, P. (1956) *Nature, Lond.* **177**, 1172.
Cutter, H. C., Fuller, W. W., Stocklen, J. B., Wilson, W. L. (1949) *J. industr. Hyg.* **31**, 139.
Duncumb, P. (1959) *Brit. J. appl. Phys.* **10**, 420.
Dundon, C. C., Hughes, J. P. (1950) *Amer. J. Roentgenol.* **63**, 797.
Gilson, J. C. (1960) *in* Industrial Pulmonary Diseases (edited by E. J. King and C. M. Fletcher); p. 122. London.
Gough, J., Wentworth, J. F. (1949) *J. R. micr. Soc.* **69**, 321.
Irwin, D. A. (1934) *Canad. med. Ass. J.* **31**, 135.
Oyanguren, H., Haddad, R., Maass, H. (1958) *Industr. Med. Surg.* **27**, 427.
Pendetgrass, E. P., Pryde, A. W. (1948) *J. industr. Hyg.* **30**, 119.
Reid, L. (1960) *Thorax*, **15**, 132.
Rivers, D., Wise, M. E., King, E. J., Nagelschmidt, G. (1960) *Brit. J. industr. Med.* **17**, 87.
Robertson, A. J. (1960) *in* Industrial Pulmonary Diseases (edited by E. J. King and C. M. Fletcher); p. 168. London.
— Whitaker, P. H. (1955) *J. Fac. Radiol., Lond.* **6**, 224.
Schuler, P., Cruz, E., Guijon, C., Maturana, V., Valenzuala, A. (1958) *Industr. Med. Surg.* **27**, 432.
Scott, M. J., Picken, D. Y. (1960) Personal communication. To be published.
Spencer, G. E., Wycoff, W. C. (1954) *Arch. industr. Hyg.* **10**, 295.

THE CLINICAL TONGUE

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With illustrations on plate

THE tongue is easily examined, yet investigators have had much difficulty in recording what has been seen. Furthermore, differing appearances are often inadequately classified and misunderstood. Improved colour photography now provides clearer definition of a wide range of changes in the tongue.

Although clinical signs are more valuable and convenient than laboratory tests in assessing malnutrition, only the extremes of clinical change can be detected with the naked eye. "No single sign is necessarily diagnostic, still less pathognomonic; each must be evaluated in the light of the history and of the other signs and symptoms, and other possible causes must be excluded" (Jeghers 1942).

Signs of nutritional deficiency are rarely single, and are probably not specific—e.g., angular stomatitis is reputed to be due to riboflavine deficiency, though a severe form can be caused by eating the skin of figs. Antibiotics and acute infection may both disturb nutritional equilibrium. Fissures of the tongue have been seen in a patient who had just completed a course of antibiotics, but these were only temporary.

Since deficiency states usually involve more than one nutrient, it is difficult to detect any specific lesion. But early detection of states of malnutrition is important because of possible interference with growth and efficiency (mental and physical), and because of its effect on susceptibility to infections, and on repair and ageing.

Severe mental effects (profound misery) can accompany the advanced stages of kwashiorkor, and one would expect that minor gradations of this mental disturbance may arise. The contribution of subclinical malnutrition to human misery and political agitation may be considerable.

Closer definition of differences in clinical appearance and their classification are therefore extremely important. It is my purpose here to clarify some of these aspects in relation to the human tongue, and to comment on factors which may be concerned in their ætiology.

The Study

My interest in clinical signs of the tongue as indicators of nutritional status was stimulated by Prof. Sidney L. Kark in the Health Centres Service of the Union Health Department. I here present the records of 1953 examinations of the tongue, which I made as part of complete physical examinations, in natural light.

Some of the variations in the clinical appearance of the tongue are illustrated in figs. 1–12. Except for those of the medical students, the photographs are the result of bed-to-bed inspection on a single morning in some of the wards of Groote Schuur Hospital. To compare the incidence of the various appearances of the tongue in separate communities, which are all in the low-income category, they have been grouped as follows:

1. The Thaba 'Nchu Health Centre, in the Orange Free State, provides a comprehensive (excluding hospital) service to a population of about 8000 Bantu in a native reserve 650 miles north-east of Cape Town. The reserve is at an altitude of 4915 ft. and the average rainfall is 22 in. per annum. The staple diet is maize (corn). People there live in brick or mud dwellings in semi-urban conditions. Malnutrition is rife in the area: 14 cases of kwashiorkor and 75 of rickets were diagnosed in a calendar year during the present survey. The data are for 1421 subjects who were completely examined physically (table I). Many of these attended child-welfare sessions for weighing, immunisation, or antenatal care, and they were not ill.

2. Motlatla is a school in Thaba 'Nchu in which practically all the scholars were surveyed on two afternoons at an interval of a week.

3. The children who did not attend school were sought out in Thaba 'Nchu in an endeavour to procure evidence for a commission on school feeding. Controls of similar age and sex were selected from schoolchildren.

TABLE I—AGE-DISTRIBUTION OF 1421 SUBJECTS COMPLETELY EXAMINED AT THE HEALTH CENTRE

Age-group (yr.)	Males	Females	Total
0–4	159	175	334
5–14	248	430	678
15–44	117	233	350
More than 45 ..	18	41	59
Total ..	542	879	1421

4. Zwelitsha is a new industrial township for Bantu people in the Cape Province, 650 miles due east of Cape Town, and 350 miles south of Thaba 'Nchu. The data presented are of an examination of every 4th child in the school registers.

5. The European children were displaced persons from Central Europe.

6. The families, all from a less privileged suburb of Cape Town, are described in more detail in the section on Familial Incidence.

Clinical Signs

The Normal Tongue (figs. 1 and 2)

Filiform papillæ, which vary in length from 1 to 3 mm., cover the anterior two-thirds of the dorsum, giving a whitish velvety appearance to the normal tongue (Cheraskin and Binford 1956). The surface is normally homogeneous, and the papillæ extend to the margins of the tongue.

The fungiform papillæ, which are barely visible, are found more often at the sides and apex of the tongue. On the dorsum they are scattered sparsely and irregularly. They are red, large, round, and smooth, and, under certain conditions, they show up prominently against the filiform papillæ.

The circumvallate papillæ demarcate the junction of the anterior two-thirds and posterior third of the tongue. Their fascinating structure has been described by Livingston (1956), and Guth (1957) caused their atrophy by sectioning the glossopharyngeal nerve. They seem to be little affected by disease (Deeny 1958).

LEGENDS TO ILLUSTRATIONS ON COLOUR PLATE

DR. HIRSCHOWITZ

Fig. 3—Normal stomach.

Fig. 4—Acute gastric ulcer (erosion).

Fig. 5—Gastroenterostomy.

Fig. 6—Five views of contraction waves in normal duodenal cap moving towards sphincter which closes the apex.

Fig. 8—First acute duodenal ulcer seen in situ by the fiberscope: the dark spot is the ulcer surrounded by œdema.

Fig. 9—Acute duodenal ulcer: the lesion is the yellowish spot with the red lower margin.

Fig. 10—Acute duodenal ulcer. The crater is in the bottom left segment.

Fig. 11—Chronic duodenal ulcer.

Fig. 12—Chronic duodenal ulcer with folds radiating from bottom left.

Fig. 13—Indolent duodenal ulcer, the large dark triangular area. Chronic duodenitis.

DR. HIRSCHOWITZ: ENDOSCOPIC EXAMINATION OF THE STOMACH AND DUODENAL CAP WITH THE FIBERSCOPE

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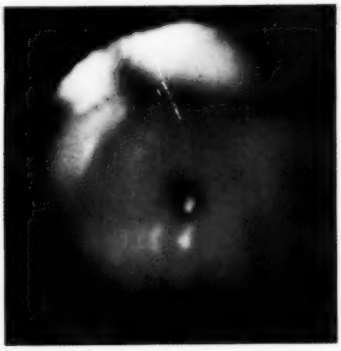

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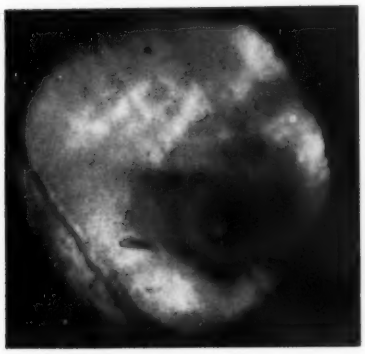

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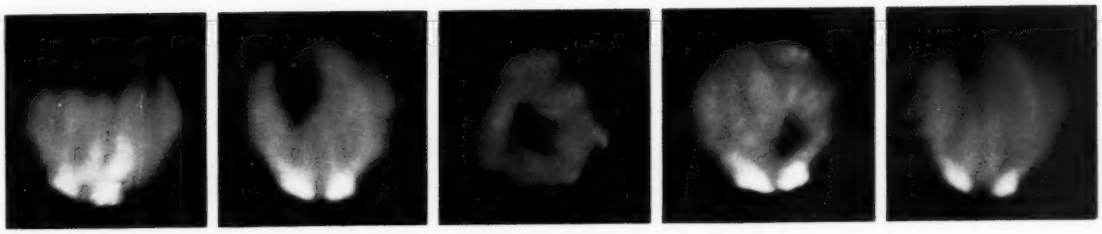

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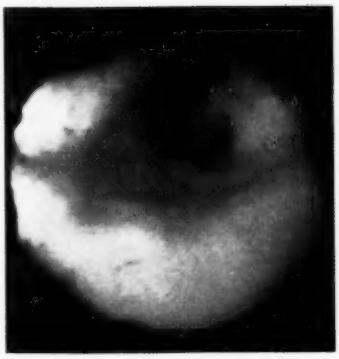

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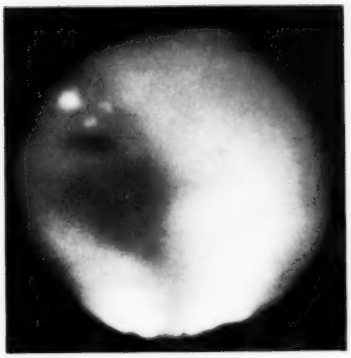

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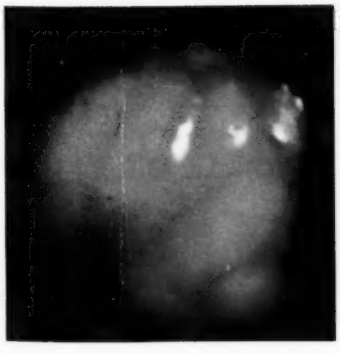

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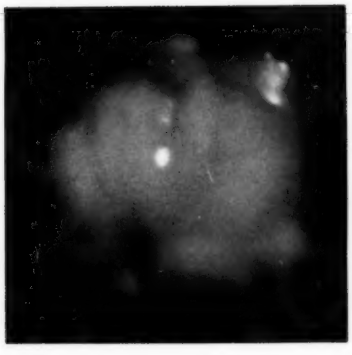

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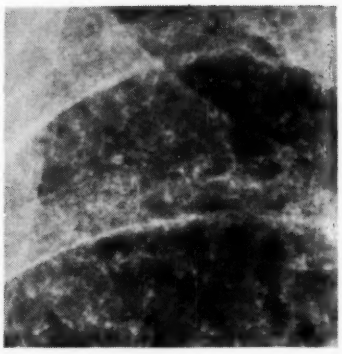
13

DR. ROBERTSON AND OTHERS: STANNOSIS

Fig. 1.

Fig. 2.



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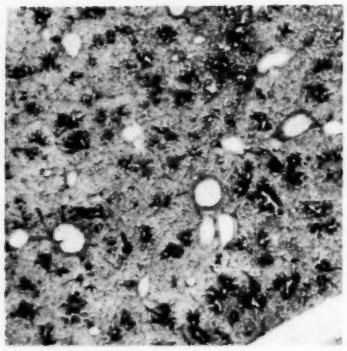

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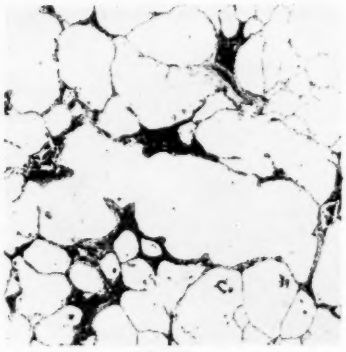

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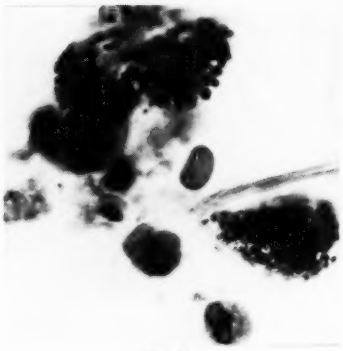

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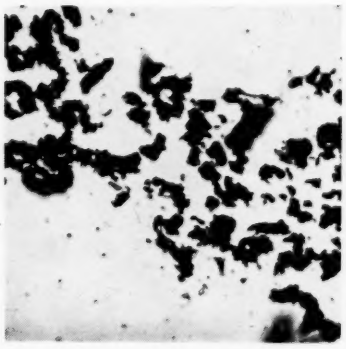

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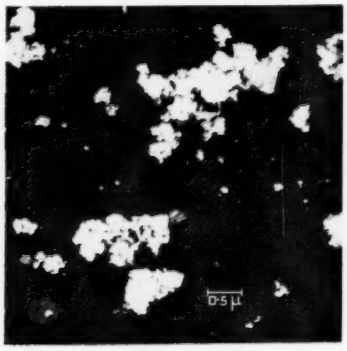


Fig. 8.

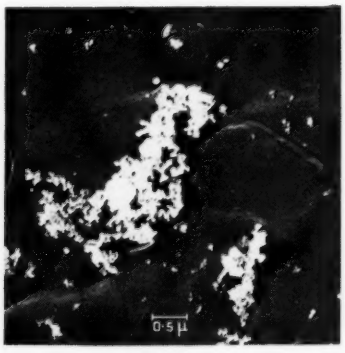
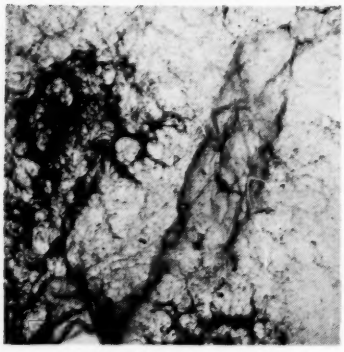


Fig. 9.



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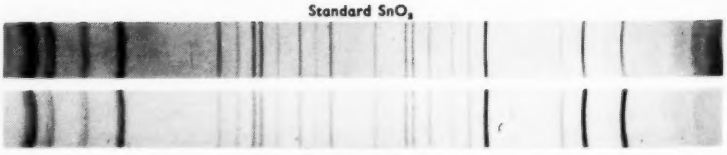


Fig. 11—X-ray-diffraction spectrum of SnO_2 and of tinworker's lung.

Fig. 1—Furnace tapping.
Fig. 2—Chest radiograph (patient no. 1).
Fig. 3—Right upper lobe. Close-up from fig. 2.
Fig. 4—The lung (paper section).
Fig. 5—Histological appearances. (Hæmatoxylin and eosin × 23.)
Fig. 6—Alveolus with dust cells. (× 1000.)
Fig. 7—Microincineration. (× 300.)
Fig. 8—Lung dust. (× 10,000.)
Fig. 9—Fume from furnace taphole. (× 10,000.)
Fig. 10—X-ray photomicrograph (25 kV). (× 6.)

DR. BROOKES AND OTHERS: CAPILLARY CIRCULATION IN BONE CORTEX

Fig. 1—A-P radiograph of right shoulder of man aged 52, showing the "spray effect" (S) in deltoid muscle after injection of hypaque in watery solution through needle inserted in acromion process.

Fig. 2—A-P radiograph of left shoulder of man aged 67, showing the "spray effect" (S) after postmortem injection of hypaque and indian ink into acromion process.

Fig. 3—A-P radiograph of left elbow of man aged 67, showing a "spray effect" produced by postmortem injection of hypaque and indian ink into lateral epicondyle of humerus.

DR. BLAU AND MR. LOGUE: INTERMITTENT CLAUDICATION OF CAUDA EQUINA

Fig. 4.

Fig. 5.

Fig. 4—Case 3: Lateral view of myelogram showing incomplete block at L3/4 disc space with linear filling defects above.

Fig. 5—Case 5: Anteroposterior view of myelogram showing incomplete block at L3/4 and L4/5 disc spaces with characteristic appearance of thickened nerve-roots at upper level.

DR. MACIVER AND DR. PARKER-WILLIAMS: APLASTIC CRISIS IN SICKLE-CELL ANÆMIA

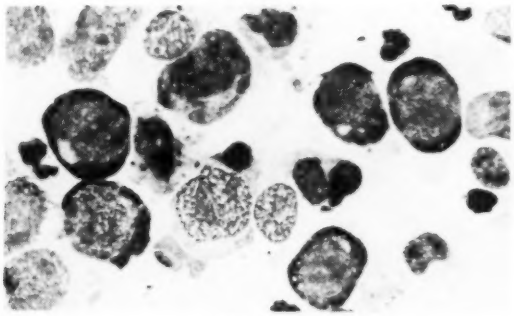


Fig. 1.

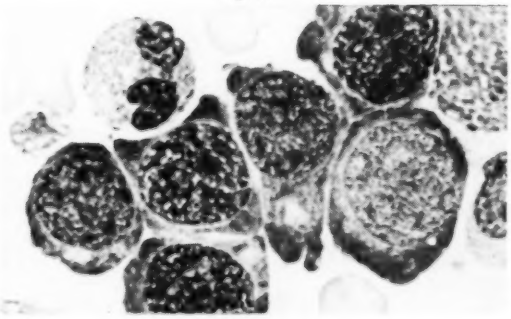
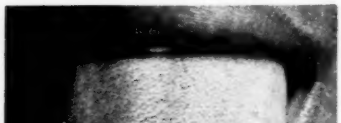


Fig. 2.

Fig. 1—Bone-marrow from case 2 on admission showing a clump of proerythroblasts: note absence of more mature cells of erythroid series. (Reduced from ×1050.)

Fig. 2—Bone-marrow from case 5 showing group of proerythroblasts and early normoblasts. (Reduced from ×2000.)

DR. KAPLAN: THE CLINICAL TONGUE



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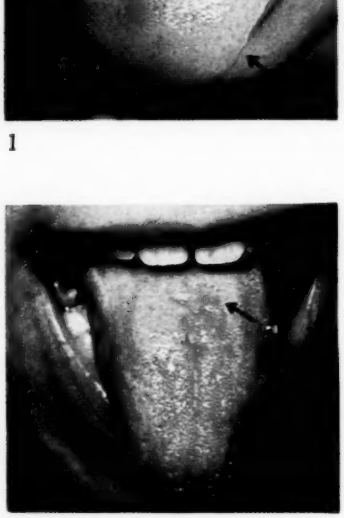
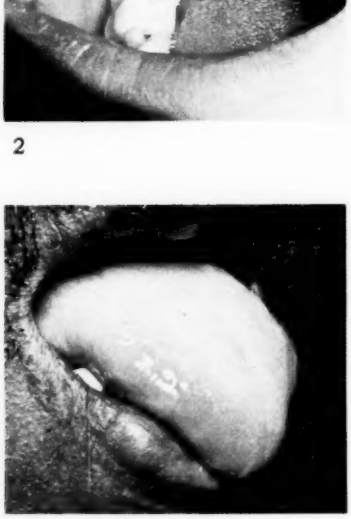


4



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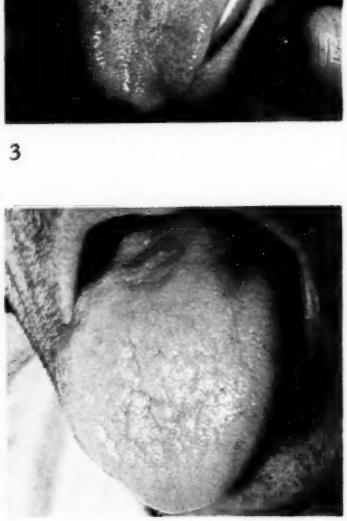

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11

12

Yeasts form the bulk of the debris, deposits of which compose the " fur " on the tongue (Deeny 1958) (see figs. 3 and 4). Loudon (1956) has cast doubt on the significance of fur. As the mobility of the posterior part of the tongue is restricted, the filiform papillæ there desquamate less readily, and so appear denser. Similarly, in paralysis of half of the tongue, the coating may be heavier on the paralysed side (Jeghers 1942).

Gandevia and Hossack (1955) have graded changes in the tongue and labelled these 0 to IV. They state that swelling, œdema, and marginal indentation are the earliest stages, but Jeghers (1942) and Jolliffe et al. (1950) first mention other lesions. In my opinion, it is better to describe the clinical appearance as an essential preliminary to studying the progression of changes.

Atrophy

I have seen obvious atrophy of the filiform papillæ of the tongue in a baby aged three months. In the early stages, papillæ at the apex and sides of the tongue desquamate leaving a smooth shining surface (fig. 5), and as a result the fungiform papillæ may appear more prominent. Later the entire surface of the tongue becomes red or " beefy ", and œdema and marginal indentation may appear. Furrowing or fissures may (figs. 6 and 7) or may not (Ekbom 1950) be associated with atrophy. Atrophy of the filiform papillæ also results in absence of fluorescence to ultraviolet light (Squires 1958).

LEGENDS TO ILLUSTRATIONS ON COLOUR PLATE

DR. KAPLAN

Fig. 1—A normal tongue with a cluster of fungiform papillæ at the left tip, marked by the arrow.

Note the homogeneous velvety " fur " extending to the margins, and the delicate pattern of furrows at the edges. The effects of lighting are shown in the contrast between the two sides of the tongue, the fungiform papillæ being visible on the right dorsum.

Fig. 2—A normal tongue, with a buccal frieze of mucous membrane of the cheek marked by the arrow.

Fig. 3—Pigmentation restricted to some of the hypertrophied fungiform papillæ.

Note that, as shown by the clear gums, the rest of the mucous membrane of the mouth is not pigmented. The centre of the tongue is furred.

Fig. 4—A geographic tongue with a defined area of " stripping " of the filiform papillæ (marked by the arrow).

Note the central fissure, and the fur. The fungiform papillæ are prominent.

Fig. 5—Early atrophy and redness of the edges of the tongue, with loss of filiform papillæ, and slight marginal indentation.

Fig. 6—Generalised atrophy of tongue with (? secondary) furrowing.

Note the absence of fungiform papillæ, and of marginal indentation.

Fig. 7—Generalised atrophy of tongue with furrowing and a central fissure (? congenital).

A European patient with macrocytic anæmia.

Fig. 8—Gross prominence of the fungiform papillæ in a healthy medical student.

Note that the filiform papillæ are not atrophied.

Fig. 9—Pigmentation of the gums which was not associated with pigmentation of the tongue.

Fig. 10—The tongue of a healthy medical student: the geographic areas of stripping of the filiform papillæ are particularly well shown.

Fig. 11—The tongue of the same student as in fig. 10, showing gross indentation of the margins.

Note the deep central fissure, other furrowing, the geographic areas, and the prominent fungiform papillæ.

Fig. 12—The tongue of the same student as in figs. 10 and 11, a year later. The geographic areas have disappeared, and the tongue shows generalised atrophy of the filiform papillæ, with prominence of the fungiform papillæ.

Ziskin and Stein (1948) have shown atrophy of the epithelium of the tongue in animals fed on a diet deficient in protein, and Gandevia and Hossack (1955) consider that atrophy of the filiform papillæ, associated with lowering of the serum-albumin level, provide a sensitive index of the patient's state of nutrition in relation to protein. Pellagra is noted for a fiery scarlet tongue which responds dramatically to treatment with nicotinic acid within twenty-four to seventy-two hours, as described by Jeghers (1942), who believes that swelling and redness at the margins and tip are the early stages, and that atrophy of the dorsum develops only later, while eventually there may be ulceration.

He thinks that atrophy of the tongue is a very valuable clinical sign, indicating some form of nutritional deficiency. He refers to the aphorism " Raw red tongue, raw red gut ".

Idiopathic steatorrhœa and sprue are often associated with atrophy of the epithelium of the tongue, and in both these conditions the tongue usually reverts to normal after treatment with ventriculin or liver. Atrophy is also found in chronic dysentery, jejunostomy, intestinal stricture, dibothriocephalus infestation, and with achlorhydria (Jeghers 1942).

Iron deficiency is accepted as a cause of atrophy of the epithelium and so is pernicious anæmia (Adams 1957). Cheraskin and Binford (1956) consider that hyperthyroidism and hypothyroidism both produce atrophy of the tongue. Squires (1958) mentioned changes in the tongue in easily diagnosed states of cardiac and nephritic œdema, and in cachexia, such as found in pulmonary tuberculosis. By means of his staining technique, he has demonstrated regeneration of papillæ after appropriate treatment.

Unduly Prominent Filiform Papillæ

The filiform papillæ are rarely enlarged. " Black hairy tongue " (Winer 1958, Stockdale 1959, Cheraskin and Binford 1956) is rare except in patients who are taking antibiotics.

Prominent Fungiform Papillæ

Prominence of the fungiform papillæ has been seen at the age of two months, and it is reasonable to infer that it may be found in the newborn. In some it may be hereditary, but it is perhaps more likely to reflect the state of nutrition of the mother during pregnancy. The appearance is often accompanied by bright red pinpoints at the apex of the tongue (fig. 1); these may be minute fungiform papillæ.

Jolliffe et al. (1950) regard hypertrophy of the fungiform papillæ as the first stage of chronic glossitis. Jeghers (1942), on the other hand, suggests that the fungiform papillæ are rendered more prominent by atrophy of the filiform papillæ which normally veil them. Squires (1953) states that in dietary deficiency there is no change in the number of fungiform papillæ. The question of true hypertrophy of the fungiform papillæ therefore remains to be elucidated (fig. 8).

The " raspberry " tongue of scarlet fever is a typical example of desquamation of the filiform papillæ, with prominent fungiform papillæ. The latter are also prominent in ariboflavinosis, but there is no proof of any relation between ariboflavinosis and scarlet fever (Jeghers 1942). In ariboflavinosis, the conspicuous fungiform papillæ convey a " mushroom " or pebbled appearance, and other signs—e.g., cheilosis and seborrhœic dermatitis—are

TABLE II—INCIDENCE OF CLINICAL SIGNS OF THE TONGUE

—	Thaba 'Nchu, Orange Free State *					Zwelitsha, Eastern Cape	European	Cape Town (families)
	Health centre *		Motlatla school	Non-school	Controls			
	Males	Females						
No. of subjects in sample	542	879	174	35	53	96	52	122
Atrophy of filiform papillæ (%)	55	57	39	60	55	59	69	35
Severe form (%)	17	14				..	..	..
Prominent fungiform papillæ (%)	73	77	88	97	79	93	38	60
Severe form (%)	12	19		43	26			
Fissures and furrows (%)	4·2	4·0	..	..	..	..	..	16
Marginal indentation (%)	7·3	10·4	..	..	..	..	..	2·5
Pigmented papillæ (%)	5·7	7·9	13	6	4	15	0	1·6
Fur † (%)	7·5	7·0	..	..	..	..	..	..

* See text. † Patients acutely ill were excluded.

almost constantly found (Jeghers 1942). The capillaries of the tongue are said to be dilated, and the tongue is painful, and of a magenta hue (Jolliffe et al. 1950), but I have great difficulty in detecting such colour gradations.

Other conditions in which the fungiform papillæ are said to be prominent are measles, diabetes mellitus, and pellagra (Cheraskin and Binford 1956).

Pigmentation

Pigmentation, which may affect the tongue in several ways, has been seen in 2 girls aged four and five years. An area of epithelium may be stained blue or brown (fig. 9), or pigmentation may be confined to the fungiform papillæ (fig. 3). Pigmentation of the papillæ is not associated with pigmentation of other mucous membranes in the mouth, nor have I seen it in Addison's disease. Its significance is unknown, but the incidence seems to vary in different communities.

Geographic Tongue

This condition, known also as erythema migrans, was first described by Rayer in 1831 (Rahamimoff and Muhsam 1957). A localised area of atrophy, or desquamation, of the filiform papillæ is demarcated by a clear greyish border; these areas are bright red in colour and may arise on an otherwise " normal " tongue (figs. 4 and 10). The earliest age at which this lesion has been identified is five years.

Jeghers (1942) and Jolliffe et al. (1950) state that geographic tongue may be hereditary, and that it may reflect a constitutional neuropathic background. The lesions vary in size and with time (Jeghers 1942, Cheraskin and Binford 1956). Rahamimoff and Muhsam (1957) have described an association with seborrhœa and spasmodic bronchitis, but not with eczema. They consider that there is a connection between geographic tongue and the subsequent development of fissures on the tongue.

Geographic tongue must be distinguished from median rhomboid glossitis—a red plaque in the midline just anterior to the circumvallate papillæ. This lesion is congenital, and it is found in 0·25% of the population (Cheraskin and Binford 1956).

Marginal Indentation

The lateral margins of the tongue are often irregular in outline and scalloped, apparently, as a result of being moulded by the teeth. This has given rise to the suggestion that marginal indentations are due to œdema, but the tongue is seldom enlarged. The condition is frequent in acute glossitis and in pellagra, but it may be quite unassociated with oral inflammation, cardiac disease, or renal disease (fig. 11).

Jeghers (1942) regards swelling and redness at the margins as early signs of pellagra; Bolton (1955) thinks that œdema of the tongue is the first stage, leading to raw edges and to fissuring. I take the view that marginal indentation is, as a rule, a late phenomenon.

Fissures

A longitudinal deep central fissure is relatively common (fig. 12), and may be congenital, especially when not associated with other signs. Some fissures are clearly the result of trauma—e.g., in epilepsy. Others, particularly when transverse, appear to be transient. Fissuring of the tongue has been seen in a child aged four years, and in another aged seven.

Severe atrophy of the dorsum of the tongue is often accompanied by fissuring of the surface and by longitudinal ridging (figs. 6 and 7) (Squires 1953). Jolliffe et al. (1950) think the fissures are caused by papillary fusion and the separation of clusters of papillæ. Jeghers (1942) thinks that fissuring may be associated with ariboflavinosis, but mentions that 0·5% of all normal age-groups have congenital fissures of the tongue. The condition is sometimes associated with hyperchlorhydria, with atrophy, and with excess of fungiform papillæ.

Another form of fissuring (i.e., plicated tongue or scrotal tongue), in association with Melkersson's syndrome, has been described by Ekbom (1950). In this condition of recurrent paralysis of the facial nerve, and recurrent œdema of the face (Klaus and Brunsting 1959), the papillæ of the tongue do not seem to be atrophied.

Variation with Time

A medical student came for routine medical examination at the Students Health Service on Aug. 30, 1956. He had no physical signs of disease, but his tongue had a deep central fissure with several " geographic " areas. The tongue looked the same in April, 1957. In June, 1959, he complained of recurrent sore throats, and his tongue was then grossly fissured, with marginal indentation and prominent fungiform papillæ. During July he was given penicillin, and later tetracycline. Figs. 10 and 11 show the appearance of his tongue on Aug. 2. Furrowing of the dorsum of the tongue is seen in fig. 10. The central fissure, marginal indentation, geographic areas, and prominent fungiform papillæ are shown in fig. 11. In February, 1960, he stopped smoking 20–25 cigarettes per day, and on June 17, when his tongue was photographed again (fig. 12), the

TABLE III—INCIDENCE OF TONGUE SIGNS IN MEMBERS OF FAMILIES

—	Total	A families*	H families*	F families*
No. of families	20	5	9	3
No. of members	122	34	57	21
Atrophic filiform papillæ (%)	35	76	28	24
Prominent fungiform papillæ (%)	60	38	88	86
Pallor (%)	11	15	1·7	9·5
Fissures and furrows (%)	16	12	30	67
Geographic areas (%)	5·7	5·9	1·8	4·8
Indentation (%)	2·5	2·9	3·5	0

* See text.

geographic areas had disappeared. Investigation of his diet is proceeding. He has not had any vitamin supplements.

Incidence of Clinical Signs

Sex and Age

Table II shows that the incidence of clinical signs in the tongue varies among communities much more than between the sexes within a community.

The age-incidence in the 1953 cases in Thaba 'Nchu has not been analysed in detail, but preliminary analysis indicates that:

1. Prominence of the fungiform papillæ is not affected by age.
2. Atrophy of the filiform papillæ is relatively unusual in childhood up to the age of four years.
3. Fissuring and marginal indentation was not detected before the age of four years.
4. Pigmentation of fungiform papillæ is unusual before four years of age, and it may appear in females slightly earlier than in males.

Incidence in Families

Lingual signs often present in a pattern which is common to several members of a family. This was shown during routine physical examinations in an attempt to investigate all members of families which were being studied by medical students as part of their training in social medicine. I conducted all the examinations in the presence of the student concerned:

Twenty families (122 subjects) were studied (table III). The five A families were selected because the majority of their members showed atrophy of the filiform papillæ. In the H families the majority of members had prominent fungiform papillæ. Fissures of the tongue were found in most members of F families.

No family qualified for both A and H groups. The difference in incidence of atrophic filiform papillæ between the two groups gives further evidence of distinct family patterns. In family no. 77, of 7 members, the filiform papillæ were atrophied in 6, and in none of them were the fungiform papillæ prominent. But it is not unusual to find both atrophied filiform and prominent fungiform papillæ in the same patient (fig. 12).

Two families (with 10 and 7 members respectively) were eligible for both H and F groups. Both conditions were found in 9 of the 10 members of family no. 39. Geographic tongue was found in 2 members of the same family only once. Prominent fungiform papillæ are unusual in anæmic patients (note the number with pallor in each group).

Of the 20 subjects with fissuring of the tongue, 14 were grouped in three families. Thus this feature shows a very definite familial tendency.

Several factors might explain why many families show a characteristic pattern. The signs might be constant and hereditary, but it seems much more likely that members of a family share their basic diet and "cultural inheritance" (Wilson 1960). Individual variations, particularly in the under-privileged groups studied in this investigation, might be due, for example, to meals away from home or food fads. "Observer error" is always an important consideration.

Unfortunately there has been no opportunity for qualitative or quantitative dietary investigation. These would be particularly valuable in comparing families with, and families without, a certain clinical sign.

A Shorthand Method

The following is a simple method of recording clinical findings:

A for atrophy of the filiform papillæ:
- A1—the atrophy is confined to tip and lateral margins (fig. 5).
- A3—the entire tongue is stripped and raw (figs. 6 and 7).
- A2—between A1 and A3.

F for fissuring:
- Central F—a central longitudinal fissure only (figs. 4 and 11).
- F1—two or three $^1/_4$-in. fissures, usually transverse.
- F3—gross fissuring of the entire tongue surface (figs. 6 and 7).
- F2—intermediate (fig. 11).

H for prominence (hypertrophy) of the fungiform papillæ:
- H1—Prominent pinpoint red spots (not raised) at the apex of the tongue only (fig. 1).
- H2—papillæ the size of a pinhead, and raised above the surface.
- H3—severe form of H2 (fig. 8).

I for marginal indentation:
- I1—mild rounded irregularity (ridging) of the edges (fig. 5).
- I3—all edges of tongue seem to have had areas bitten out (? moulded by tooth projections) (fig. 11).
- I2—intermediate.

N for pallor of tongue (? anæmia):
- N1—mild.
- N2—intermediate.
- N3—gross pallor (? severe anæmia).

P for pigmentation of fungiform papillæ:
- P1—1–3 pigmented follicles.
- P2—3–6 pigmented follicles.
- P3—7+ or a cluster (fig. 3).

A pigmented plaque, "fur", and "black hairy tongue" should be recorded in longhand.

The tongue in fig. 5 would thus be recorded as "A1, I1", and in fig. 7 as "central F, A3, F3".

Conclusions

Research is still urgently needed, and many questions remain:

1. Are these signs affected by season and do they vary with time? Can they be altered with vitamin supplements? Prominence of the fungiform papillæ could easily be studied with these problems in view.
2. What are the stages of recovery of a tongue in which filiform and fungiform papillæ have been grossly atrophied? Feeding experiments in schools seem indicated.
3. What are the microscopic features of pinpoint and pinhead fungiform papillæ? Are they hypertrophied?
4. What are the microscopic features of marginal indentation? Is œdema present?

Summary

The results of clinical (macroscopic) examination of the tongues of 1953 patients reveal a great diversity of appearance, which is illustrated by colour photographs.

The differences seen are classified, and the frequency of each type of lesion in several communities and families is described. It is suggested that the wide variations in incidence between the groups are due to environmental (including nutritional) influences.

A shorthand method of recording the clinical appearance of the tongue is presented.

I am indebted to Mr. B. Todt for the photographs; to Mrs. D. Cleary and Mrs. S. Klein for statistical assistance; and to Prof. R. Singer for criticising this paper.

REFERENCES

Adams, J. F. (1957) *Lancet*, i, 1120.
Bolton, J. H. (1955) *Med. J. Aust.* i, 10.
Cheraskin, E., Binford, R. T. (1956) *Pediat. Clin. N. Amer.* **3**, 919.
Deeny, J. (1958) *J. Irish med. Ass.* **42**, 103.
Ekbom, K. A. (1950) *Acta med. scand.* **138**, 42.
Gandevia, B., Hossack, D. (1955) *Med. J. Aust.* i, 344.
Guth, L. (1957) *Anat. Rec.* **125**, 715.
Jeghers, H. (1942) *New Engl. J. Med.* **227**, 221.
Jolliffe, N., Tisdall, F. F., Cannon, P. R. (1950) Clinical Nutrition; pp. 33, 53, 76. New York.
Klaus, S. N., Brunsting, L. A. (1959) *Proc. Mayo Clin.* **34**, 365.
Livingston, R. M. (1956) *Ann. R. Coll. Surg. Engl.* **19**, 185.
Loudon, I. S. L. (1956) *Brit. med. J.* i, 18.
Rahamimoff, P., Muhsam, H. V. (1957) *A.M.A. J. Dis. Child.* **93**, 519.
Stockdale, C. B., Banks, L. L. (1959) *Practitioner*, **182**, 215.
Squires, B. T. (1953) *Trans. R. Soc. trop. Med. Hyg.* **47**, 329.
— (1958) *Cent. Afr. J. Med.* **4**, 104.
Wilson, C. (1960) *Lancet*, ii, 1078.
Winer, L. H. (1958) *A.M.A. Arch. Derm.* **77**, 97.
Ziskin, D. E., Stein, G. (1948) cited by Roth, H. *Oral Surg.* 1959, **12**, 830.

Reviews of Books

Surgical Diseases of the Pancreas

JOHN M. HOWARD, M.D., F.A.C.S., professor and chairman, department of surgery, Hahnemann Medical College, Philadelphia; GEORGE L. JORDAN, JR., M.D., M.S., F.A.C.S., associate professor of surgery, Baylor University College of Medicine, Houston. London: Pitman Medical Publishing Co. 1961. Pp. 606. 147*s*.

THIS book radiates an aura of solid wealth. To start with inessentials, it is superbly produced. The paper, the print, the diagrams, the radiographs, even the two coloured plates (so often reminders of the limitations rather than the scope of medical illustration) are a joy: the illustrations are plentiful without swamping the pages and beautifully executed with none of that strip-cartoon gaudiness which besets some books. A first glance reveals a store of clinical material and almost unlimited means to make full use of it. Time as well as talent must have been lavished on the clipped clear sentences which, almost on any page, carry the reader tirelessly from one paragraph to the next. The formidable lists of references at the end of each chapter bespeak, at the very least, an impeccable library service. The price, by British standards, is high. One almost hesitates to plunge more deeply into such a book: is it not almost bound to disappoint? This one does nothing of the sort.

Both Dr. Howard and Dr. Jordan are international authorities on pancreatic diseases; and they have gathered around them a small but select group of helpers. (Their list starts alphabetically with Edwin E. Ellison who writes on what is now widely known as the Zollinger-Ellison syndrome; and it ends with Kenneth Welch and Allen O. Whipple, the latter contributing a "historical sketch".) The result of their labours could be called monumental if, besides size, impressiveness, and solidity, the adjective did not imply something static and unchangeable. The very opposite impression is conveyed: pancreatic surgery emerges from this book as a rapidly expanding subject in which new ideas abound and new ventures are encouraged. At the same time—and in this respect the work is exhilaratingly American—time-honoured but unsound or disproved notions have been mercilessly eliminated or at least critically re-examined. Characteristically Dr. Howard's brilliant chapter on the ætiology of acute pancreatitis carries the subtitle Facts and Fancies; and past, present, and future fellowship candidates will meet with as many friends among the "fancies" as among the "facts". Indeed, many will feel reluctant to part with so much hard-earned intellectual investment (guilt-edged one had fondly imagined), were it not that so much that is new and stimulating is offered in its place.

British readers will be most grateful perhaps for the sections on the rarer forms of pancreatitis—especially the chronic, relapsing, and alcoholic varieties—which are less commonly seen in this country than in America. An encyclopædic but streamlined review of the various islet-cell tumours should prove helpful to those specially interested in this rare but fascinating condition. In short, a splendid book which every hospital library should possess.

Quantitative Cellular Hæmatology

J. M. YOFFEY, D.SC., M.D., F.R.C.S., professor of anatomy, University of Bristol. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961. Pp. 122. 44*s*.

THIS book is a compressed account of the work on the quantitative aspects of the formation and fate of the cells in the blood and bone-marrow that Professor Yoffey has already given in larger books and in many papers. Most hæmatologists know that Professor Yoffey and his coworkers believe that, in the guineapig at least, there is now considerable evidence in support of Maximow's hypothesis that the lymphocyte can act as a stem cell for the development of cells of other series, particularly the red cells and the granulocytes. Short accounts are given of the various experimental approaches that have led Professor Yoffey to this conclusion, and they provide an excellent means for readers to form their own conclusions about the validity of the results without having to delve into a mass of papers. The book also illustrates the techniques now available in studies of this kind. Unfortunately these techniques are hard to apply to the human subject, and the stumbling-block of species difference stands in the way of translating Professor Yoffey's results into terms of human pathology and physiology without some supporting evidence. What little supporting evidence exists is quoted here; but it is the experimental biologist rather than the clinical hæmatologist who will find this monograph worth studying.

Procedures in Vascular Surgery

RICHARD WARREN, M.D., clinical professor of surgery, Harvard Medical School, Boston. London: J. & A. Churchill. 1961. Pp. 211. 85*s*.

THERE can be few medical cities where the criteria of good practice are more strictly examined than Boston, Mass., and when a new monograph appears from the Peter Bent Brigham Hospital we can be sure that mature reflection on sound evidence is its basis. Dr. Richard Warren here records his own methods which he has found to work well in most of the standard peripheral vascular problems of today. By line drawings and concise written directions he takes his readers step by step through such diverse operations as resection of an abdominal aortic aneurysm to stripping and ligation of varicose veins. Practical hints are liberally, even generously given, in a way not always common in this type of work. Positioning of the patient, for example, is very usefully shown; and so are those many little difficulties and delaying factors that beset the path of the less experienced worker. Now that some skill in this kind of specialty is expected of any general surgeon, this book should find a ready welcome among them. Postgraduate students of surgery and operating-theatre staff will also be helped by it. Vascular surgeons will find many points of interest to them, and little to disagree with.

The Eye and Its Function

R. A. WEALE, PH.D., D.SC., senior lecturer and head of the department of physiological optics, Institute of Ophthalmology (University of London). London: Hatton Press. 1960. Pp. 209. 55*s*.

IN this book there is much varied information and wide discussion of some aspects of modern experimental work on vision. The writing is so clear that no-one should have difficulty in understanding even the unfamiliar. Many people can surely learn something from this book, but some may wonder for whom it was actually written: the expert will know most of the answers already; for the man already interested in ophthalmology much of the book will seem elementary; for the medical undergraduate there are too many details, though the definitions of simple terms suggest that it is meant for beginners. Nevertheless, for anyone who is ignorant of this subject and has time for reading outside his own immediate area, the book will be interesting and profitable. The clear type, excellent illustrations, and intelligible discussions give pleasure.

Principles of General Neurophysiology Relating to Anæsthesia and Surgery (London: Butterworth. 1960. Pp. 136. 21*s*.).—This reprint of a chapter by Dr. B. D. Wyke from *General Anæsthesia* by Dr. Frankis Evans and Dr. Cecil Gray deals with a subject that may become of value to many anæsthetists. The later part of the work will be of greatest interest to present-day anæsthetists and surgeons, for it discusses the blood-supply to the brain. Dr. Wyke describes how this and other factors are related to the brain's oxygen supply, and he includes a helpful section on the cerebrospinal fluid. Although the book makes no claim to be comprehensive, this section could perhaps be expanded to give practical details of such procedures as electroencephalographic monitoring of anæsthesia. Anæsthesia is described as "a controlled, reversible intoxication of the nervous system", and this book will do a considerable service if it impresses on its readers the delicacy of the structures which it is the business of the anæsthetist to intoxicate.

THE LANCET

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Compensation for Cupidity?

THE law relating to compensation for injuries well illustrates the limitations of an abstract concept of justice. If one person suffers injury as the result of the negligence of another it is held to be just and reasonable that the injured person should be compensated by the person at whose hands he has suffered the injury. We take it for granted—hardly noticing the assumption—that this compensation must take the form of money; and the courts have established a kind of tariff by which they can assess the monetary value, not only of a finger, a leg, or an eye, but even of a dead man's loss of enjoyment of the remainder of his life, which his widow may be entitled to receive. But here the law at present draws the line: only civil negligence carries these implications, and if someone murders her husband he is not compelled to compensate her.

The law cannot, save in exceptional circumstances, be kept waiting beyond the normal delay of a few years between the accident and the award of compensation. However difficult the doctors may find it to say what will be the ultimate fate of the injured man, and though one may assert that he will be back at work in three months while another says that he will never work again, the judge must decide this issue at the time of the trial. If the events show that he erred in giving the plaintiff £10,000 too much or too little, nothing can be done about it afterwards.

Lawyers and doctors who practise in the courts have long known that these considerations apply with special force to compensation awarded for traumatic neurosis. A person who has sustained an injury complains of symptoms not present before it, not due to any discoverable organic lesion, and leading to incapacity. The doctor decides that these symptoms are due to a neurosis, which is held to be a form of illness. The law then says that this illness is attributable to the accident, and entitles the victim to compensation.

Dr. HENRY MILLER, in his recent Milroy lectures,[1] has drawn fresh attention to the drawbacks of this system. It has, of course, long been recognised that traumatic neurosis is highly selective in its incidence: it occurs rarely in those who are not entitled to compensation for their injuries from someone else, and only in certain groups of those entitled to compensation. MILLER provides statistical support for a view which has long been held by many doctors: that the large majority of victims of compensatable traumatic neurosis make a rapid and complete recovery when their claim is disposed of—win or lose. This being so, it may be argued that one of the causes of such traumatic neurosis is the expectation of compensation, and that the law is paradoxically compelling one party to compensate another for a consequence of his act which the law itself has created, and that it is therefore inflicting an injury on the defendant, and adding to his injury, by assessing the compensation that he has to pay on a scale which events may show to be quite excessive. The law, however, may well retort that the remedy is in the hands of the doctors. It is after all a doctor who says that the injured man or woman is suffering from "an illness". Perhaps it is time that this idea was re-examined. Leaving "compensation neurosis" on one side for the moment, where should the line be drawn between an illness and the conscious elaboration of complaints? Is the "hysterical" housewife who tyrannises over her household through her symptoms ill? And what of the patient who boasts of her incurability, and the number of doctors her "illness" has defeated? It is often said that hysterical symptoms serve an unconscious purpose; but this is self-contradictory, for there can be no purpose without at some point a conscious direction of the will. Has "illness" the same meaning when applied to appendicitis and hysteria, and can a broken leg and "compensation neurosis" be described in the same sense as the results of an injury?

These questions go to the root of human responsibility and challenge ideas propagated by the analytical psychologists which today perhaps we are too apt to take for granted. The opposite view is expressed by BARRETT[2] writing of the French existentialist, SARTRE:

> "The essence of man, according to the French thinker, lies not in the Œdipus complex (as Freud held) nor in the inferiority complex (as Adler maintained); it lies rather in the radical liberty of man's existence by which he chooses himself and so makes himself what he is. Man is not to be seen as the passive plaything of unconscious forces, which determine what he is to be. In fact, SARTRE: denies the existence of an unconscious mind altogether; wherever the mind manifests itself, he holds, it is conscious. A human personality or human life is not to be understood in terms of some hypothetical unconscious at work behind the scenes and pulling all the wires that manipulate the puppet of consciousness. A man *is* his life, says Sartre; which means that he is nothing more nor less than the totality of acts that make up that life."

Most commentators on MILLER's observations have said gloomily that, although they may be true, there is nothing the law can do about it; and MILLER[3] himself has pointed out that the procedure under the old Workmen's Compensation Acts which provided for the indefinite payment of weekly compensation, subject to periodical assessments of the injured workman's recovery, merely prolonged the neurosis indefinitely. One reason for this was the knowledge that after several years of weekly compensation both parties were often equally glad to be rid of the case by means of a lump-sum settlement.

But if the law is bad, it will not improve itself: that is a matter for Parliament. Most lawyers perhaps fail to recognise how far social practice has already sapped away the theoretical basis of the law of compensation for

1. *Brit. med. J.* April 1, 1961, p. 919; *ibid.* April 8, p. 992.

2. Barrett, W. Irrational Man. London, 1961.
3. *Times*, April 24, 1961.

civil injuries. For in most cases it is no longer the party responsible for the injury who pays the compensation, but a particular social group, acting collectively through insurance companies; and this collective responsibility is in some cases enforced by law. So the motor-drivers collectively compensate the victim of one of their number, and the employers the injured workman, for whatever firm he works. In fact the motor-car insurance companies have so far departed from the idea of justice that when no third party is involved they divide the cost of an accident between them (" knock for knock ") even though one party, who may be entirely innocent, is unjustly penalised by the loss of his no-claim bonus. The State itself has an indirect interest in all this, since unless an injured person is compensated from some other source he becomes a charge on social insurance; and even then there is a subtle distinction between industrial disease and ordinary illness which is reflected in a difference in the scale of benefit.

These are certainly difficult problems, but it is surely clear that the law of compensation for injury has become in some respects antisocial, and that the development of collective and social responsibility has outmoded legal concepts of justice in this field. Has the time not come for a Government inquiry?

Tuberculosis in Children

IN 1930 the Brompton Hospital established the first special child contact clinic in Britain. To the early reports by DOW and LLOYD,[1–3] who founded the clinic, and subsequent ones by MACPHERSON and her colleagues,[4–10] a complete account of twenty-five years' study has now been added by DAVIES.[11] This merits close attention; for, although much has been published on many aspects of childhood tuberculosis, the natural history of the disease in children has been little studied. A long-term investigation such as this is not easily carried out: for it requires not only special facilities but also tenacious interest.

The survey covers 2377 children who had been in contact with tuberculous patients in the years 1930–1952, when, in general, neither B.C.G. nor chemotherapy was available. Of this total, 1567 were infected with tubercle bacilli. In nearly half of these, clinically or radiographically detectable tuberculous lesions developed; and 25 died from miliary tuberculosis or pulmonary tuberculosis.

The main fact that emerges from the report is the paramount importance of age at first infection in determining the subsequent clinical pattern of tuberculosis. For instance, in infants active tuberculosis developed in 3 out of 4 after their initial infection, and 1 in 4 died from this; whereas in adolescents less than half (40%) of those infected developed active tuberculosis, and only 1 in 50 died. The age at the time of infection was shown to determine the type of lesion. Thus, the younger the child, the larger the lymph-node component of the primary complex and the more commonly did the disease become disseminated. Massive lymph-node enlargement in early life led commonly to segmental or lobar lesions due to obstruction of bronchi by the nodes. A third of the pulmonary lesions in infants were segmental or lobar, whereas in adolescents only 1 in 14 were of this type. Further evidence of the importance of hæmatogenous dissemination in early life was found in the high incidence of extrathoracic lesions in infants. Nearly half (45%) of all infected infants developed such lesions, whereas less than 1 in 50 (1·5%) of the 535 children infected during adolescence developed extrathoracic complications, and not a single adolescent developed miliary tuberculosis. Equally striking was the lung component of the primary complex in older children: in almost a tenth (8%) of children infected in adolescence " adult type " lesions developed; whereas in no child infected in infancy has this type of disease yet developed, though many of these patients have been followed up well into adult life. The older the child the more commonly did pleural effusion follow primary tuberculous infection. No pleural effusions were found among the infected infants, whereas effusions occurred in association with 7% of all thoracic lesions in adolescents.

A review of the chest X-rays taken at the children's first visit showed that a tenth of all calcified opacities proved to be " active " and that in a further 5% " active " tuberculous lesions developed elsewhere. No opacity without calcification was found to be " inactive ", and a review of the chest X-rays of those with primary lesions showed that in over 90% visible calcification developed. In almost a quarter of the segmental lesions there was no calcification—presumably owing to the caseous contents of the nodes being extruded into the bronchi and coughed up. This is an important observation, because it emphasises that the absence of calcification does not exclude tuberculosis as the cause of such abnormalities as bronchiectasis, bronchostenosis, or unilateral emphysema.

The prognosis for segmental or lobar lesions was found to be good; for, although half the children were left with anatomical abnormalities, only 1 of the 76 had by 1952 developed symptoms attributed to such abnormalities, and only 1 subsequently had " adult-type " tuberculosis. This, however, represents too hopeful a view; for a subsequent investigation of 51 children attending the same clinic [10] with this type of initial lesion showed that, by 1960, 7 had required surgical treatment, 5 of them for lower-lobe bronchiectasis. In general, children with visible primary lung lesions were twice as likely subsequently to develop " adult type " disease as those who never had such a visible lesion. This increased predisposition is confined to certain types of lesions—namely, pleural effusion and primary lesions with abnormal lung components (e.g., massive or multiple primary foci).

1. Dow, D. J., Lloyd, W. E. *Brompton Hosp. Rep.* 1932, **1**, 20.
2. Dow, D. J., Lloyd, W. E. *Brit. med. J.* 1931, ii, 183.
3. Dow, D. J., Lloyd, W. E. *ibid.* 1932, i, 701.
4. Lloyd, W. E., Macpherson, A. M. C. *ibid.* 1933, i, 818.
5. Wingfield, R. C., Macpherson, A. M. C. *ibid.* 1936, i, 741.
6. Lloyd, W. E., Macpherson, A. M. C. *ibid.* 1936, ii, 1131.
7. Macpherson, A. M. C. *Brit. J. Tuberc.* 1939, **33**, 79.
8. Macpherson, A. M. C. *Brit. med. J.* 1943, ii, 98.
9. Macpherson, A. M. C., Lutwyche, V. U. *Thorax*, 1950, **5**, 1.
10. Macpherson, A. M. C., Zorab, P. A., Reid, L. *ibid.* 1960, **15**, 346.
11. Davies, P. D. B. *Tubercle, Lond.* 1961, **42**, suppl.

DAVIES makes some tentative suggestions for the management of child contacts. He points to the dangers from miliary tuberculosis in early life, and to the likelihood of " adult type " disease in late childhood; and he notes that, whereas miliary tuberculosis almost always occurs within a year of the first infection, " adult type " tuberculosis always occurs more than a year after the first infection. From this it follows that long follow-up is necessary for older children, especially those who have had a pleural effusion or unusual primary infections, those with a strong family history of the disease or continued contact with it, and those with high tuberculous sensitivity. Treatment is advisable probably for all who are thought to have been recently infected and certainly for all with manifestly " active " lesions.

In some ways this study, which is largely statistical, resembles that carried out by BRAILEY [12] as part of the Harriet Lane study of tuberculosis in white and Negro children in Baltimore. But some of the findings differ considerably. The incidence of extrathoracic lesions in white children is approximately the same in both series (Davies 2·9%, Brailey 3·7%) but in Negro children BRAILEY found it to be 7%. The mortality in DAVIES'S series was 6% in infected infants who were untreated, whereas in BRAILEY'S series it was under 3% in white children and only 1% in Negro children. The behaviour of the disease is likely to differ between different parts of the world and different races; but differences have also been recorded between fairly comparable series in a single country. For example, of children under 5 years of age extrathoracic tuberculosis was found in a third by CAMMOCK and MILLER [13] in Newcastle and in almost half by SHAW and WYNN-WILLIAMS [14] in Bedford, but in only just over a tenth by DAVIES at Brompton. The differences depend largely on differences in selection of material and in methods of assessment. In addition the natural history of tuberculosis may vary between different communities in the same country, though there is no conclusive evidence of this. Certainly, however, the exact pattern of childhood tuberculosis in one community should not be inferred from that in another; and there is need therefore for further large-scale studies on the lines of these at Brompton Hospital. It is particularly important that such studies should be undertaken in the economically less favoured countries, where both racial and environmental conditions may differ greatly from those in countries where the most extensive investigations have hitherto been made. The influence of chemoprophylaxis and B.C.G. vaccination in preventing infection of exposed children, and of chemotherapy in preventing spread of infection once it has occurred, are being examined in several countries. Ideally such studies should be based on properly designed trials, such as that carried out with isoniazid by the U.S. Public Health Service [15] and by LINCOLN.[16] But controlled trials are sometimes impossible, owing to either lack of facilities or ethical considerations; and in these circumstances much valuable information can be obtained by accurate and long-continued clinical observation as in the Brompton Hospital series.

12. Brailey, M. E. Tuberculosis in White and Negro Children. Cambridge, Mass., 1958.
13. Cammock, R. M., Miller, F. J. W. *Lancet*, 1953, i, 158.
14. Shaw, J. R., Wynn-Williams, N. *Tubercle, Lond.* 1956, **37**, 243.
15. U.S. Public Health Service Tuberculosis Therapy Trial. *Amer. Rev. resp. Dis.* 1959, **80**, 627.
16. Lincoln, E. M., Harris, L. C., Bovornkitti, S., Carretero, R. W. *Amer. Rev. Tuberc.* 1958, **77**, 39.

Treatment of Renal Bone Disease

IN 1946 ALBRIGHT and his colleagues [1] distinguished a particular form of renal rickets or osteomalacia which they were able to cure with alkalis and vitamin D. The responsible renal disease, called by them " renal tubular insufficiency without glomerular insufficiency " and now commonly known as " renal tubular acidosis ", had not usually caused nitrogen retention or gross glomerular damage when the bone disease was recognised. Subsequently, other forms of renal osteodystrophy, such as the rickets complicating cystine storage disease [2] and the osteomalacia of the adult Fanconi syndrome,[3] have been shown to respond to similar therapy. In these conditions disorder of renal tubular function is more obvious than is damage to the glomeruli with impairment of the kidneys' excretory function. All these conditions are rare; but bone disease can be detected histologically in about two-thirds of all patients who die of renal failure,[4 5] and in some with chronic uræmia the bony changes may produce the clinical features of rickets, osteomalacia, or hyperparathyroidism. These more common forms of renal osteodystrophy have been neglected therapeutically, even though more than twenty years ago GRAHAM and OAKLEY [6] showed that azotæmic renal rickets could apparently be cured by administration of alkalis with vitamins A and D. There has also been a singular lack of interest in the possible mechanisms by which destructive renal disease or " renal glomerular insufficiency " causes defective skeletal mineralisation; and the careful metabolic studies of LIU and CHU [7] have suffered general neglect by the experts on metabolic bone diseases.

Recent independent but parallel investigations by DENT, HARPER, and PHILPOT [8] and by STANBURY [9] are of therapeutic and theoretical interest. Both groups of workers claim symptomatic relief and apparent clinical cure of bone disease in patients with chronic uræmia by treatment with vitamin D, and their claims are supported by convincing radiographic evidence of healing rickets and osteomalacia. Neither subscribes to the popular belief that metabolic acidosis is primarily concerned in the pathogenesis of azotæmic osteodystrophy; and neither found that alkalis affected mineral metabolism or the state of the bones; both effected clinical cure with vitamin D in patients with untreated acidosis. Dihydrotachysterol, calciferol (vitamin D_2), and cholecalciferol (vitamin D_3) appear to be equally effective clinically, but

1. Albright, F., Burnett, C. H., Parson, W., Reifenstein, E. C., Jr., Roos, A. *Medicine, Baltimore*, 1946, **25**, 399.
2. Bickel, H., Smallwood, W. C., Smellie, J. M., Hickmans, E. M. *Acta paediat., Stockh.* 1952, **42**, suppl. 90, p. 27.
3. Saville, P. D., Nassim, F., Stevenson, H., Mulligan, H., Carey, M. *J. Bone Jt Surg.* 1955, **37B**, 529.
4. Berner, A. *Helv. med. acta.* 1944, **11**, 741.
5. Follis, R. H., Jr., Jackson, D. A. *Bull. Johns Hopk. Hosp.* 1943, **72**, 232.
6. Graham, G., Oakley, W. G. *Arch. Dis. Childh.* 1938, **13**, 1.
7. Liu, S. H., Chu, H. I. *Medicine, Baltimore*, 1943, **22**, 103.
8. Dent, C. E., Harper, C. M., Philpot, G. R. *Quart. J. Med.* 1961, **30**, 1.
9. Stanbury, S. W. *in* Recent Advances in Renal Disease (edited by M. D. Milne). London, 1960.

each must be given in amounts much greater than are required to cure nutritional rickets. As in hypophosphatæmic vitamin-D-resistant rickets, the need for large doses of vitamin D involves the hazard of overdosage and hypercalcæmic intoxication. The individual patient may apparently have an unpredictable minimal dosage requirement, and huge doses (up to 200,000 I.U. [5 mg.] of calciferol daily) may sometimes be given without producing either clinical benefit or detectable metabolic effect.[9 13] This particular problem can be solved only by metabolic balance measurements; and, although general therapeutic rules can be formulated,[8] there is much to be said for treating these cases in centres with resources for making such measurements.

The metabolic data from these uræmic patients are of interest in that the external mineral balances mimic the state in simple vitamin-D deficiency. In the untreated patient the fæces contain approximately the same amount of calcium as is taken in the diet, and the urinary calcium is negligible; the metabolic response to treatment with vitamin D resembles closely the response when nutritional rickets is treated with much smaller doses of the vitamin. In the light of the lead given by LIU and CHU,[7] these observations have been taken to suggest that in renal failure some factor interferes with the biological activity of vitamin D.[8 9] Nothing is yet known of the mechanism of this apparent antagonism; but the curative effect of vitamin D in renal osteodystrophy does not seem to be mediated through change in the Ca×P ionic product in the plasma.[9]

Osteitis fibrosa is present in all cases of azotæmic osteodystrophy,[10] even when the chief abnormality is rickets or osteomalacia, and it is nowadays thought to be caused by secondary hyperparathyroidism.[11–13] Both DENT [8] and STANBURY [9 13] have detected radiographic evidence of healing of the characteristic cortical erosions [14] of secondary hyperparathyroidism during effective treatment with vitamin D. BALL,[15] comparing the histological appearances of bone from uræmic patients who had died after protracted treatment and of bone obtained by biopsy before treatment was started, has shown that osteitis fibrosa is apparently reversible by vitamin-D therapy. Whereas the London workers [8] advocate treatment of renal hyperparathyroidism with vitamin D, those in Manchester have criticised this as dangerous,[12] and have resorted to parathyroidectomy (which is obviously also potentially dangerous) before giving vitamin D to these patients.[13] The difference is largely one of semantics, since the former group rely on radiographic appearances for the diagnosis of renal hyperparathyroidism, whereas the latter restrict the term azotæmic hyperparathyroidism to cases in which the bone shows no histological evidence of defective mineralisation, "the skeletal changes being dominated by osteitis fibrosa and extensive remodelling and replacement of lamellar by woven bone".[10] Patients of this strictly defined group consitute a small minority of all cases of azotæmic osteodystrophy: the bony changes are indistinguishable from those of primary hyperparathyroidism,[16] the parathyroid glands are usually greatly hyperplastic, the plasma-phosphate is high and the plasma-calcium near normal, and metastatic calcification is especially liable to develop spontaneously.[17] Possibly the parathyroid glands in this syndrome become autonomously hyperfunctional (as apparently occurred in a case of chronic steatorrhœa previously reported by DENT[18]) in which event large doses of vitamin D may not cure the renal osteitis fibrosa. But whether the parathyroid glands are autonomous or not, treatment with vitamin D would tend to raise further, and dangerously, the already high plasma levels of calcium and phosphate. Consequently, in the exceptional patient with bone changes of this type, in whom the renal failure appears not to be rapidly advancing, parathyroidectomy may be indicated before starting treatment with vitamin D.[13]

Investigation of this fascinating group of disorders should throw new light on the physiology of vitamin D and of the parathyroid glands, especially when simpler techniques for vitamin and hormonal assay come to hand. At present, cases investigated in different centres can be compared only if the histological state of the bone is known precisely. Thus it is to be hoped that a carefully defined procedure for bone biopsy will be followed by all studying this problem.

10. Ball, J. *in* Recent Advances in Pathology (edited by C. V. Harrison). London, 1960.
11. Gilmour, J. R. The Parathyroid Glands and Skeleton in Renal Disease. London, 1947.
12. Stanbury, S. W. *Brit. med. Bull.* 1957, **13**, 57.
13. Stanbury, S. W., Lumb, G. A., Nicholson, W. F. *Lancet*, 1960, i, 793.
14. Pugh, D. B. *Amer. J. Roentgenol.* 1951, **66**, 577.
15. Ball, J. Personal communication.
16. Albright, F., Reifenstein, E. C., Jr. The Parathyroid Glands and Metabolic Bone Disease. London, 1948.
17. Herbert, F. K., Miller, H. G., Richardson, G. O. *J. Path. Bact.* 1941, **53**, 161.
18. Davies, D. R., Dent, C. E., Willcox, A. *Brit. med. J.* 1956, ii, 1133.

Annotations

TELEVISION IN THE MEDICAL SCHOOL

LAST week the Postmaster-General made public his reasons for not acceding to the B.B.C.'s request for permission to operate a limited service of colour television; and about the same time the Association for the Study of Medical Education (ASME), at its conference at the London Hospital Medical College, was also hearing, though with rather different explanations, why some people feel that colour television in medical teaching and research has not yet reached the stage for confident advance and spending of money. Indeed the conference (its programme imaginatively arranged by the medical committee of the Scientific Film Association) had almost as much to tell about impediments to the effective use of television in the medical school as about its positive powers. But the meeting provided an informative examination of a relatively new and complex instrument of teaching and research; and ASME is ably fulfilling its purpose in stimulating thought and debate on this sort of enterprise —where enthusiasm may run as far as funds permit before it has looked very carefully where it is going. Enthusiasm, however, seldom fails to meet scepticism; and, as Dr. John Ellis, the Association's secretary, related, the proposal to hold a conference on television in the medical school had its opponents ("No, I still prefer the personal approach");

but if the doubters were many their voices were few last week, and the main message of the meeting was that, despite technical misgivings and questions about details of application, television has a place in the medical school as an extension of the power and range of the teacher—though never as a dominating technique.

Thus, the quality of the teacher mattered more than the mechanism of his teaching, declared Prof. Roger Warwick, the Guy's anatomist, who has been among the most active examiners of television as a teaching medium in British medical schools (he took a large share in organising the colour demonstration of medical teaching from Alexandra Palace in 1957 [1]). Last week a black-and-white screening of a dissected hand illustrated how a good teacher's scope could be extended beyond the few students who would ordinarily benefit from such a demonstration. It would clearly have been more impressive in colour; but the key question was whether the more forceful teaching impact would justify the expense and technical hazards of a colour installation. Professor Warwick was more cheerful about the outlook for colour (for one thing, " black and white must always be second best ") than the American visitors, who had evidently had some dispiriting experiences. Dr. Murray C. Brown spoke of the financially disastrous efforts to reach a fully satisfactory colour system in the United States and of the troubles medical teachers had had in getting simple black-and-white systems to meet their needs at a price they could afford. And Dr. David S. Ruhe, of the University of Kansas School of Medicine, unhesitatingly favoured the use of the elementary and cheaper black-and-white until the emergence of exotic colour in more practical terms. Dr. E. W. Bird, of the Naval Medical Center across the way from Dr. Brown's headquarters at the National Institutes of Health in Bethesda, painted a humorous picture of the distractions of colour, with viewers arguing that reproduction was too red or too blue and rather forgetting what it was all about. Five years ago, he said, almost everyone forecast that today colour would be the thing, but they had been very wrong. But like his colleagues he was much impressed by a film, shown to the conference by Dr. Brian Stanford, illustrating several forms of endoscopy televised in colour by a small two-colour camera developed by Minot in Marseilles. The colour range of this camera might not be adequate for other work, but here it seemed a big advance on those " giant creatures " (as Dr. Ruhe called them) at present necessary for full-scale colour reproduction. The conference also saw something of the exciting prospects made visible by fibre optics and the flexible fiberscope (the subject of Dr. Hirschowitz's article on p. 1074) which will be an added stimulus to achieve cheaper and simpler colour television. So the present phase of despondency about colour and its expense may not last long.

The cost of installing a one-camera colour system in an operating-theatre may be as great as that of equipping ten or more theatres with monochrome cameras [2]; but the medical school with a little money to spend on television teaching experiments might be able to invest a few hundred pounds in black-and-white equipment. No elaborate studio was needed (Dr. Ruhe was stern about those who declared that television teaching must have a special studio); and there were many advocates of " on the spot " television in operating-theatre, laboratory, or lecture-theatre, with audience and demonstrator in direct touch, in contrast to most people's idea of television teaching by a remote figure at some distance from his screenbound students. Using another technique, relatively simple equipment was sufficient for the demonstration, by Dr. David Stafford-Clark and Dr. B. L. Mallett, of how to preserve the privacy of a psychiatric interview and yet enable a large audience to look and listen in. " Merely an expensive substitute for the one-way-vision screen " was one comment; but other responses were more favourable. For this kind of teaching, black-and-white seemed fully adequate. Again in dental teaching, with its emphasis on practical methods, television can display small operative details to large audiences; and this subject seems as certain as any to expand its use of television.

" Medicine and dentistry still have a major task of sorting through the many remarkable items and gadgets of the commercial, educational and industrial television worlds to see which items of paraphernalia and which techniques of visualisation might serve their needs." [2] They have indeed: and the teachers must establish as they go along that the introduction of a new television technique can always be justified by offering a definite advance over films, slides, and other aids to teaching. As the ASME conference was at pains to emphasise, the fascinations of electronics must not become too beguiling.

1. See *Lancet*, 1957, ii, 1126.
2. Bird, E. W., Connolly, D. A. Medical-Dental TV Reference. American Medical Association (Communications Division), 1961.

ELECTRICAL ANÆSTHESIA AGAIN

IN theory the induction of anæsthesia by electricity has much to commend it; for it does not involve the use of potentially harmful drugs, and depends neither on continued lung ventilation nor on an intact circulation for the distribution and elimination of the anæsthetic agent. In practice, however, experience with electrical anæsthesia has not been encouraging. D'Arsonval used electric currents to produce unconsciousness in animals as long ago as 1890.[3] Over the years the most satisfactory technique proved to be the passage of an alternating current of some 25–75 milliamperes with a frequency of some 700–1500 cycles per second [4]; to maintain the same depth of narcosis the strength of the current had to be increased as time went on. There were many difficulties. A current of this intensity caused pain at the point of its first application. Moreover it often produced generalised muscular contractions, amounting in some instances to a frank convulsion. In laboratory animals these movements interfered both with the patency of the upper airway and with the contractions of the respiratory muscles, and quite commonly anoxia ensued; parasympathetic overactivity manifested itself as bradycardia and salivation; cardiac irregularities were usual.

Knutson et al.[5] applied this method to man. They overcame some of the difficulties by premedication with atropine, and they administered gallamine triethiodide to control excessive muscle movement. They found, as had Hertz,[6] that there were no reliable signs of anæsthesia: indeed the current might render the patient immobile and yet not insensible. Tachycardia, hypertension, and cardiac irregularity were sufficiently prominent and severe for Knutson et al. to be unwilling to continue the work. Those who used electronarcosis for the treatment of

3. Cited by J. T. Gwathmey. *Anæsthesia*, 1914, p. 628.
4. Knutson, R. C. *Anesthesiology*, 1954, **15**, 551.
5. Knutson, R. C., Tichy, F. Y., Reitman, J. H. *ibid.* 1956, **17**, 815.
6. Hertz, J. *Rev. path. comp.* 1933, **33**, 385.

psychiatric illness seem to have reached a similar conclusion.[7 8]

After four years' study of electrical anæsthesia in dogs Hardy et al.[9] felt that they had overcome these difficulties and could go on to use the method in man. They now report two cases in which the initial discomfort of the passage of the current was successfully overcome by administration of a short-acting barbiturate, and in which the muscle movements were controlled by suxamethonium. Total myoneural block was not induced, and the return of spontaneous respiration was used as an indication that anæsthesia was becoming too light. Though salivation was pronounced, no cardiac arrhythmia, tachycardia, or hypertension was noted. Tracheal intubation and assisted pulmonary ventilation were, of course, necessary.

If this work is confirmed, and particularly if the return of spontaneous respiration in fact proves a reliable sign of imminent return of consciousness, electrical anæsthesia may prove clinically useful.

DISSEMINATED SCLEROSIS

EPIDEMIOLOGICAL studies of chronic diseases are arduous but often rewarding,[10] and disseminated sclerosis is no exception. Even with due allowance for the difficulties in establishing uniform diagnostic criteria, there is an impressive weight of evidence that the disease is more prevalent in the cold and temperate higher latitudes of Europe and North America than in their southern parts. Just conceivably this difference may be determined racially rather than climatically; for the northern populations studied tend to be weighted with people of Scandinavian ancestry. In England neither onset nor exacerbation of the disease varies seasonally.[11] It is well established that multiple cases are found in more than 6% of affected families. There are, however, so many reported instances in which only one of identical twins has been affected [12] that common exposure seems a likelier explanation of familial incidence than hereditary endowment: the possibility of a genetic factor in ætiology is not supported by blood-group studies.[13] On the other hand conjugal cases are exceptional, suggesting that any influence of common exposure may be exerted only in youth. Clinical experience confirms that the disease is sometimes activated and even apparently initiated by exogenous factors, including infection and prophylactic inoculation. About a third of acute exacerbations follow overt but often banal and non-specific infections.[13] The association with prophylactic inoculation is rare but well authenticated.[14]

Ideas on causation have ranged from the incrimination of "suppression of insensible perspiration" [15] to a preoccupation with autoimmune mechanisms.[16] Experimental studies of the allergic encephalomyelitis which can be provoked in some laboratory animals by the injection of brain emulsions [17] have created fascinating problems of their own; but the analogy of this disorder with disseminated sclerosis is questionable. The experimental lesion seems to be closely related to that found in the human perivenous demyelinating encephalomyelitis which occasionally complicates measles or smallpox vaccination, but the relation of all these acute lesions to the chronic disease is more disputable. The experimental studies have gained new significance from the important observations of Uchimura and Shiraki,[18] who demonstrated massive demyelination and marginal gliosis in patients who had died of chronic encephalitis following treatment of rabies. In these cases the lesions were strikingly similar to those in subacute disseminated sclerosis. This finding has revived hopes that the basic pathological processes in disseminated sclerosis can be investigated indirectly through the medium of experimental allergic encephalitis, and both the experimental and the human disease are now being subjected to extensive immunological and immunochemical studies.

Clinically the application of the controlled therapeutic trial [19] is a welcome development, even though its initial contribution has proved negative. It seems likely that tolbutamide, intrathecal tuberculin, and long-term steroid therapy will shortly join the motley procession of discarded remedies, though short-term steroids may possibly find a place in the treatment of acute exacerbations.[13] Ironically the humble aspirin, employed apparently as a second "control" by Miller and his colleagues,[19] is the only "treatment" which, judged statistically, is even marginally beneficial; and its apparent effect is of theoretical rather than practical importance.

ELECTROLYTES IN HUMAN UTERUS

THE myometrium is a peculiar muscle in that its structure and function are largely controlled by ovarian hormones. This relationship has been found whatever properties of the muscle have been studied—growth and development, tension response, or content of contractile proteins and organic phosphate compounds.[20] Experimental work suggested that variations in these properties are associated with changes in the electrolytes both of the myometrium and of the endometrium,[21] and it has long been suspected that one mechanism by which ovarian hormones act on uterine muscle is by regulation of the internal ions. Subsequent experimental studies on animals have given conflicting results, and some of the original findings have not been confirmed.[22] A report by Hawkins and Nixon [23] on the effects of ovarian hormones on human myometrium is therefore particularly welcome.

These workers took biopsy specimens from non-pregnant patients with and without hormone administration (5 control, 4 after œstrogen). Their principal finding is that, on a dry-weight basis, the œstrogen group showed an increase in both water and sodium content; and, since the chloride was unchanged, it was concluded that these effects were intracellular. There was no change in potassium. These results in general resemble those originally reported in the immature rat.[24] The sodium and water content of the human myometrium is known to increase

7. Kalinowski, L. B. *Dig. Neurol. Psychiat.* 1949, **17**, 296.
8. Rees, W. L. *J. ment. Sci.* 1949, **95**, 162.
9. Hardy, J. D., Fabian, L. W., Turner, M. D. *J. Amer. med. Ass.* 1961, **175**, 599.
10. Allison, R. S. *Proc. R. Soc. Med.* 1961, **54**, 1.
11. Schapira, K. *J. Neurol. Psychiat.* 1959, **22**, 285.
12. Mackay, R. P., Myrianthopoulos, N. C. Proceedings of Sixth International Congress of Neurology, 1957, sect. 8, **10**, suppl. p. 24.
13. Miller, H. *Proc. R. Soc. Med.* 1961, **54**, 8.
14. Palffy, G., Mérei, F. T. *World Neurology*, 1961, **2**, 167.
15. Cruveilhier, J. Anatomie Pathologique du corps humain; vol. 2. Paris, 1829-42.
16. Miller, H. G., Schapira, K. *Brit. med. J.* 1959, **1**, 737, 811.
17. Kies, M. W., Alvord, E. C. Allergic Encephalomyelitis. Springfield, Ill., 1959.
18. Uchimura, I., Shiraki, H. *J. Neuropath. exp. Neurol.* 1957, **16**, 139.
19. Miller, H., Newell, D. J., Ridley, A. *Lancet*, Jan. 21, 1961, p. 127.
20. Csapo, A. *in* Modern Trends in Obstetrics and Gynæcology (edited by K. Bowes). London, 1955.
21. Horvath, B. *Proc. nat. Acad. Sci., Wash.* 1954, **40**, 515.
22. Bitman, J., Cecil, H. C., Hawk, H. W., Sykes, J. F. *Amer. J. Physiol*, 1959, **197**, 93.
23. Hawkins, D. F., Nixon, W. C. W. *J. Obstet. Gynæc. Commonw.* 1961, **68**, 62.
24. Talbot, N. B., Lowry, O. H., Astwood, E. B. *J. biol. Chem.* 1940, **132**, 1.

in pregnancy,[25 26] evidently owing to increased endogenous production of œstrogen. Progesterone in the doses used was found to have no notable effect on electrolytes in non-pregnant subjects.

It is to be hoped that these pioneering studies will be continued, and that enough biopsies will eventually be obtained to produce statistically convincing results. There is one serious technical difficulty in the interpretation of the findings of Hawkins and Nixon. They have based their calculations of internal ion concentrations on tissue chloride as a measure of the extracellular space. Chloride is known to penetrate many types of muscle, though the use of the uncorrected chloride space in skeletal muscle can be defended in some situations where there is good evidence that little error is introduced.[27] In the myometrium, however, this method produces results which are more questionable. On this basis the extracellular space[33 25] comes to over 60% of the muscle in non-pregnant myometrium. The intracellular potassium is taken as 28·4 mEq. per 100 g. dry-weight with intracellular water as only 96 g. per 100 g. dry weight. This gives the concentration of potassium as 296 mEq. per kg. cell water, which is double that found in skeletal muscle.

This problem has been considered by others[28] in relation to rabbit and cat uterus. Daniel and Robinson[28] reject calculations based on the uncorrected chloride space as giving intracellular concentrations which are hypertonic. They have used a modified chloride space in which allowance is made for internal chloride according to the membrane potential, as in skeletal muscle, plus some chloride which is not leached out in sucrose solution. The resulting "space" is similar to that determined with sucrose; and this gives figures for intracellular potassium which are credible. Other workers have used rapidly diffusible sodium as an extracellular marker in the rabbit uterus.[22] As regards the human myometrium, until this problem can be solved, results cannot be expressed in terms of cell content, and further progress will be delayed. It is desirable to find at least two methods which give similar results for the "space"; this has been achieved for skeletal muscle[29] and for rabbit myometrium.[21 28] There seem to be compelling reasons for this particular piece of space research.

ANAEROBES AND OXYGEN

Antony van Leeuwenhoek[30] knew that some of his "little animals" could live with little or no air, and Spallanzani[31] managed to keep one infusion alive in a high vacuum for thirty-five days. But if a professional anaerobiologist should be seeking an excuse for celebrations he could not do better than choose 1961 as being the centenary year of Pasteur's original description of the "butyric fermentation".[32] The cause of this fermentation was shown to be rod-shaped organisms. While examining a drop of fluid containing these organisms under a coverslip on a slide, Pasteur noted that those at the periphery of the drop, and therefore nearest the air, had ceased to move, while those at the centre were still moving. This simple observation led him to investigate whether air was harmful to these organisms, and he in fact showed that it was possible to inhibit butyric fermentation by passing a current of oxygen or air through the fermenting liquid. Pasteur soon discovered that this was no freak phenomenon and that several organisms responsible for putrefaction were able to live without oxygen and were killed by its presence. For such organisms he proposed the word "anaerobe".[33]

A great variety of strict anaerobes, including clostridia, anaerobic cocci, bacteroides, and spirochætes, were later shown to be responsible for human infections. It is now realised that a low oxidation-reduction potential in the environment is more important for the growth of these organisms than the complete absence of oxygen; and, provided the environment in the normal subject, in diseased tissue, or in the test-tube has sufficient reducing properties, anaerobes may flourish in the presence of a small amount of free oxygen. The presence or absence of oxygen, however, is one of the main factors determining the oxidation-reduction potential, and growth of anaerobes in general is inhibited by the presence of oxygen. In a few species quite low concentrations are actively lethal. The mechanisms of this action are obscure, though it has been suggested that since anaerobes lack catalase and certain similar enzymes they are unable to destroy toxic peroxides formed when the organisms are exposed to oxygen.

In the management of severe infections caused by anaerobic organisms many measures have been advocated to improve the oxygenation of the tissues and thus discourage the growth of the invaders. Apart from excising dead and diseased tissue, various workers have recommended local application of hydrogen peroxide and zinc peroxide, injection of peroxides into the diseased tissues, intensive general oxygen therapy through a mask, local oxygenation by encasing a limb in an airtight bag containing oxygen, and even repeated injections of oxygen directly into the tissues.

Boerema and his colleagues[34 35] in the department of surgery of the University of Amsterdam have recently carried attempts at tissue oxygenation a stage further by allowing the patient to breathe pure oxygen in a pressure chamber. Preliminary experiments on guineapigs suggested that exposure for periods of two hours to oxygen at a pressure of three atmospheres prevented or greatly diminished the infection normally produced by subcutaneous or intramuscular injection of cultures of *Clostridium welchii*. This same regime was later used in the treatment of severe human infections, including two cases of advanced clostridial myositis and a case of massive gangrene of the abdominal wall suspected of being caused by anaerobic organisms. In ordinary circumstances these patients would probably have died, but with oxygen therapy, which was repeated if necessary two or three times in twenty-four hours, all made a good recovery.

Clearly high-pressure oxygen therapy is not without its difficulties and dangers. But many doctors will be familiar with the sense of hopelessness induced by a case of advanced gangrenous disease, and it would be very good news if the encouraging results of the Dutch workers were confirmed.

25. Hawkins, D. F., Nixon, W. C. W. *J. Obstet. Gynæc. Commonw.* 1958, **65**, 895.
26. Cort, R. L., Cort, J. H. *Lancet*, 1957, i, 718.
27. Manery, J. F. *Physiol. Rev.* 1954, **34**, 334.
28. Daniel, E. E., Robinson, K. *J. Physiol.* 1960, **154**, 421.
29. Boyle, P. J., Conway, E. J., Kane, F., O'Reilly, H. L. *ibid.* 1941, **99**, 401.
30. Leeuwenhoek, Antony van. Letter to Royal Society, June 14, 1680, *in* Dobell, C. Antony van Leeuwenhoek and his Little Animals. London, 1932.
31. Spallanzani, L. Opuscoli di fisica animale e vegetabile dell' Abate Spallanzani. Modena, 1776.
32. Pasteur, L. *C.R. Acad. Sci., Paris*, 1861, **52**, 344.
33. Pasteur, L. *ibid.* 1863, **56**, 1189.
34. Boerema, I., Brummelkamp, W. H. *Ned. Tijdschr. Geneesk.* 1960, **104**, 2549.
35. Brummelkamp, W. H., Hogendijk, J., Boerema, I. *Surgery*, 1961, **49**, 299.

Needs and Beds

FAMILY FLATS WITH A NURSING ANNEXE

A Danish Experiment for the Disabled

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IN most countries hospital beds are expensive and scarce, yet many of them are filled by patients who need only care and attention. Unfortunately it seems likely that the number of these long-stay invalids will increase. We are likely to have more old people; and, with modern therapeutic methods and drugs, many people survive formerly fatal illnesses but have to live with a disability. War, traffic, and industry each claim their own casualties, and too many of these are young people.

At present completely helpless patients usually have to be in some form of institution; but in Copenhagen we have lately built an experimental block of flats with some hospital facilities on the top floor, where it is hoped they will be able to live with their families and yet not become too great a burden on their healthy relatives.

BACKGROUND

In 1952 there was an epidemic of poliomyelitis in Denmark, and for the first time a considerable number of patients survived though with respiratory paralysis. They have now been in hospital for 8 years and this has had serious consequences both for them and for their families. The young patients have lost their ties with their siblings, and some of the very young cannot remember anything except life in a hospital bed. Spouses have become estranged and some marriages have ended in divorce. There seemed to be no future for these patients other than a continuing hospital life with increasing deterioration of family ties.

However, a new venture changed the outlook for them. In 1956, as a pilot project, a few respiratory patients were discharged and placed in their own homes, with the result that the physical and emotional wellbeing of some of them improved. Even if a father breathes only through a respirator, he will want to play his part in the daily life of the family, helping to bring up the children, visit relatives and friends, and share in community life, Similarly, a paralysed child needs the love and care of his parent and siblings, and he too wants to follow the happenings in his family. Likewise the single adult, who used to have rooms of his own, usually wants to get away from a hospital life with its rigid time-table and changing nurses.

PLANS FOR INDEPENDENCE

In 1959 the National Foundation against Poliomyelitis gave 1 million Danish kroner (about £50,000)* to the Ministry of Social Affairs to provide accommodation for these patients outside hospital.

As a start all the patients and their families were interviewed by a social worker and asked to say how they thought their future should be arranged. Their wishes had to be considered against the family background, and the difficulties caused by the long separation had to be faced. Some marriages had broken up, and some were only formally still in existence. Where the patient was a child, two or three more babies had been born into the family, with whom the patient had not established any ties. The wishes of the relatives as well as the patients had to be taken into account, for we recognised that the experiment would fail unless there was honesty on both sides.

According to what was said in these interviews, the patients could be grouped as follows:

(*a*) Patients, who wanted to live alone with their family in a specially designed and equipped individual home (12 patients).

(*b*) Single patients, who for various reasons—such as divorce or death of a relative—wanted to live alone with a housekeeper-nurse in a suitable apartment (2).

(*c*) Patients who had to be placed in an institution because their relatives felt they could not accept responsibility (6).

(*d*) Patients who wanted to live with their families in private flats, but at the same time have the help of an institution (6).

The wishes of the first four groups could be met by orthodox solutions, but the groping wishes of the last group contained an idea for a new form of care. They wanted the privacy of family life in a setting which would provide a regular medical service, professional nurses, reserve respiratory equipment, and accommodation where the patients could sleep under professional supervision. As one of the parents put it, they needed *a combination* of family and institutional care.

In response to these suggestions an experimental block of flats with some medical facilities was opened in Copenhagen last summer. A semi-public organisation representing the Ministry of Social Affairs, the National Foundation against Poliomyelitis, and the Society and Home for the Crippled, has been made responsible for the management.

THE PROJECT

The project is housed in a new 13-storey block containing 170 flats and such communal services as doorman, switchboard, and restaurant. It is owned by a non-profit housing association. 14 flats are reserved for respiratory patients and their families, and the organisation pays the housing association a monthly rent of 425-800 kr. for each flat.

Each family has its own flat with bathroom, and kitchen. The flat is designed, and equipped with extra electrical equipment and safety installations, to accommodate respiratory patients.

On the top floor of the building there is a nursing annexe with professional staff and emergency equipment. It contains cubicles where patients can sleep under professional supervision at night, when they are ill, or when their families are on holiday. In an emergency a patient can be wheeled in his bed or wheelchair to an elevator and within minutes be under professional care on the top floor. The annexe also has living-rooms, a classroom for education and entertainment, and roof gardens. There are some rooms in downstairs flats for a few patients who do not have families and who must be classified as full-time institutional patients.

Staffing

In our experience a member of the family is able to look after these patients with some help from the nurses and doctors of the annexe. A mother, a wife, a sister, or a full-time housekeeper is employed by the Government to take on this responsibility after some hospital training in the use of respiratory equipment. The principle of paying a member of a family to look after a relative has never been used in Danish social welfare before. But if a

* 1 krone=1 shilling.

relative becomes a full-time paid attendant she cannot take on another job, and more than half of all married women in Copenhagen are employed outside their own home. From the point of view of the Government she replaces a nurse who would have to be paid anyway, since the expenses for the care of the severely handicapped is a State responsibility.

Finance

The benefit normally paid under the Danish disablement insurance scheme does not nearly cover the care of a patient with respiratory poliomyelitis and must be supplemented by the Government. Financial needs vary from family to family, and no flat-rate salary for taking care of a relative or flat-rate subsidy is recognised; but each case is considered individually.

In a family consisting of a sick child and her widowed mother, who after a training period in the hospital is responsible for the care of her daughter, the flat is regarded as an official flat as long as the mother takes care of the patient. Besides the rent, a monthly allowance of 700 kr. is paid to cover other expenses.

Another family consists of a father, mother, and paralysed child. The father has a job, the mother takes care of the child, and besides the rent the family is paid an allowance of 150 kr.

Single adult patients have a full-time housekeeper/nurse who gets full board and lodging in the patient's flat and a salary of 450 kr. a month. The patient gets the rent for the flat, and 350 kr. to cover his own expenses.

The institutional services (medical care, sleeping cubicles, nursing care, education, entertainment) are free of charge.

Help With Problems

It was expected that some patients and their families would meet difficulties in this new way of life. Some families had to move from the country to a big city. Sometimes the wage-earner had to get a new job, and the children had to move to new schools and find new friends. Accordingly a trained social worker, who can work intensively with the patients and with their families, is considered essential to success.

CONCLUSIONS

Though it is much too early to evaluate the results of this project, some preliminary conclusions might be drawn as to the wider application of this type of service:

1. A new type of service has been designed in an attempt to meet the growing number of patients who are severely handicapped not only by the after-effects of poliomyelitis but also by such conditions as multiple sclerosis, debilitating diseases, or old age.

2. Severely handicapped patients and their families have been enabled to function as a family unit in spite of the handicap.

3. Badly needed hospital beds and personnel have been released for other purposes.

4. Public funds have been saved, since the cost of maintaining a patient in his own home is less by a third than the cost of maintaining him in hospital.

5. For the first time the Government has employed a member of a family to look after a sick relative.

Special Articles

MEDICAL EMIGRATION

Second Thoughts on the Royal Commission

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IN April, 1958, the Royal Commission on Doctors' and Dentists' Remuneration examined the extent of medical emigration from Great Britain. The commission called evidence from the Ministry of Health, which offered figures on the migration by sea of both doctors and dentists from the beginning of 1951 to the last quarter of 1957. According to these, over this $6^3/_4$-year period, there was a gross loss to the United Kingdom of 2509 doctors and dentists. As no further evidence was taken on this subject, the commission's conclusion that "the emigration of doctors was no higher than the general rate" was presumably made on these figures, which were provided by the Board of Trade.

It is difficult, however, to see how it was reached; for if there is one doctor to each 1000 of the population—not an unreasonable assumption [1]—we should expect to find 2,509,000 people emigrating from the United Kingdom over this period. In actual fact the figure was less than a million, which suggests that the medical migration-rate was higher than the general rate. It must be remembered that the figures quoted here are gross, and that some of the 2509 doctors were returning home after working in this country as students. But if the medical migration-rate is to be the same as the general rate, over 60% of this gross figure must be accounted for by doctors returning to their homelands. This seems unlikely.

Further doubts are thrown on the commission's conclusion if we consider a Commonwealth country such as Canada. The Canadian Government prides itself on its care in screening immigrants. The following are figures obtained from the Department of Citizenship and Immigration [2]:

Years	1955	1956	1957	1958	1959
British immigrants from U.K. ..	29,228	46,135	102,994	22,439	16,604
British doctors from U.K.* ..	195	214	311	202	182

* These figures do *not* include Canadians returning to Canada after graduation in the U.K., or British doctors entering Canada from the U.S.A.

Thus, according to Canadian Government sources, 1104 British doctors have migrated to Canada during the past five years. During this period some 217,400 Britons have settled in Canada, and there is nothing to suggest that more doctors return to the United Kingdom than other members of the public. The doctor/patient ratio for emigrants is therefore 1/196 as compared with 1/1000 in this country. The medical migration-rate to Canada thus seems to be something like five times the general rate.

A detailed analysis of the figures given to the Royal Commission shows that, according to our own Board of Trade, there was a gross export to Canada of 184 doctors in 1955, 146 in 1956, and 178 during the first nine months of 1957. These figures differ so greatly from those given above that some corroboration should be sought.

As collateral evidence, I may say that the Canadian medical profession has become increasingly alarmed at the influx of foreign-trained doctors. Thus Dr. Langston, in

1. According to the Willink Committee's report of 1957, para. 15 (based also on the 1951 Census figures), there were 53,260 doctors in practice—i.e., 1 doctor to each 1000 patients in Great Britain.

2. Annual and quarterly statistical reports of the Statistics Section Department of Citizenship and Immigration. Ottawa, 1960.

his presidential address to the College of Physicians of British Columbia in 1956, called for a tightening of the registration requirements and further restrictive measures. " After all ", he remarked, " in this respect the 60 or more doctors who graduate from our university must be our concern. It is reasonable for them to look forward to an opportunity to establish themselves in their home-province if they so desire."[3] In British Columbia a British graduate is at present required to pass the Canadian finals examination, spend a period of internship in an accredited hospital, and pay fees of £125 to register. But, even so, there are now over 300 British graduates on the provincial medical register, compared with only 35 in 1948. Since 1948 almost a quarter of all registrants have been British, and a further 29 were added in 1960.

According to the Willink Committee's report in 1955 we could expect to export a total of 190 doctors per annum. Yet the figures I present here show that during the past five years an average of 220 doctors—equivalent to the whole output of two medical schools—have left the U.K. annually to settle in Canada alone. What of other countries, such as Australasia and the U.S.A. ? More have left for these countries than for Canada, according to the Board of Trade.

Lafitte and Squire,[4] in their article calling for medical-school expansion, remark: " What has actually happened to the supply of general practitioners since 1955 is not wholly clear." I feel confident that inspection of foreign and Commonwealth medical registers would reveal many of the 300 doctors we appear to be short of each year.

I conclude with two suggestions:

1. Our medical register should be reorganised so that each registrant pays an annual fee to remain on it, and is required to give information about his or her type and place of practice. This procedure, which is found in some Commonwealth countries, would enable the Government to obtain reliable statistical data.

2. Part of any money set aside for expanding our medical schools should be used for discovering why so many doctors prefer to practise abroad.

3. Presidential message of Dr. Robert G. Langston. Newsletter 13. College of Physicians and Surgeons of British Columbia. 1956.
4. Lafitte, F., Squire, J. R. *Lancet*, 1960, ii, 538.

Public Health

Infectious Diseases in England and Wales

Diseases	Week ended April				
	1	8	15	22	29*
Diphtheria	1	5	7	11	7
Dysentery	564	449	486	390	439
Encephalitis:					
Infectious	1	2	1	6	2
Postinfectious	2	6	6	7	2
Food-poisoning	97	104	123	113	170
Measles, excluding rubella	35,096	40,456	41,028	31,157	23,513
Meningococcal infection	16	19	23	21	15
Ophthalmia neonatorum	22	16	19	18	21
Paratyphoid fever	1	1	5	20	25
Pneumonia, primary or influenzal	278	312	282	257	220
Poliomyelitis:					
Paralytic	5	8	8	9	11
Non-paralytic	2	..	1	5	7
Puerperal pyrexia	118	157	172	181	168
Scarlet fever	463	434	397	330	417
Smallpox	..	..	..	..	..
Tuberculosis:					
Respiratory	355	324	429	430	417
Meninges and C.N.S.	2	3	5	9	7
Other	45	38	70	55	62
Typhoid fever	..	3	1	1	2
Whooping-cough	660	631	636	650	691

* Not including late returns.

In England Now

A Running Commentary by Peripatetic Correspondents

PONDERING about a recent exhibition of X-ray apparatus evoked a vision of an X-ray department of the future.

The radiologist was explaining that the wedding of the X-ray tube to the television camera in the 'fifties had led to an increased study of radiophysiology so that movement was now as important in diagnosis as radioanatomy. This had led to the old X-ray films and darkroom becoming obsolete, and complete automation of apparatus had made radiographers unnecessary too. The radiologist had once again become a doctor to whom patients were referred for an opinion based on his electrophysical examination. Before being placed in the apparatus, all patients to be X-rayed were seen by a radiologist in his consulting-room and interrogated to amplify the notes they had brought. The room was comfortably lit by subdued lighting and the X-ray image appeared brightly on the monitor. The only controls were for brightness and contrast and the radiation hazard was reduced to negligible proportions by the small output.

The X-ray image was recorded magnetically on videotape in its entirety, with each recording prefaced by the patient's own particular electrical code signal which allowed his tape to be rapidly identified. The tape was later reported upon by the radiologist on his reproducing monitor, and could be run either fast or slow, forwards, backwards, or stationary, and the reports were finally taped verbally in the form of a commentary. By pressing a switch at any time a still photograph of half-plate size for inclusion with the clinical notes was produced instantly by xerography, or a complete duplicate tape could be made for dispatch to another hospital or for direct transmission by telephone wire.

In large departments the less difficult cases were examined by junior radiologists in training; and in some outlying smaller hospitals the examination was made by the house-surgeon, the image being relayed to the parent hospital by landline.

Clinicians wishing to view the tape called at the X-ray library. The reproducing monitor was primed with the patient's electrical code signal, and the appropriate reel of tape ran at high speed until stopped by the code signal at the record required.

The vision faded before it could be ascertained whether only the Treasury's refusal to provide an X-ray apparatus in every ward had prevented the radiologist following his films into oblivion, or what happened when the hospital electronic engineer was on holiday.

* * *

For me, this is the best time of the year—the halcyon weeks just before the exams, when the students start to bend at the hips as I pass them in the corridors. Naturally, this has nothing to do with the fact that I am the internal examiner; it just happens that about this time of the term their innate good manners come to the surface. For the rest of the year these are fairly well submerged, and there is a regrettable tendency to elbow Sir aside at the local picture-house, if he is constituting an obstruction on the way to the ice-cream, or to pay his witticisms less than their due meed of attention. But for this fortnight nothing is too good for me; my jokes are all excellent, my arrival hushes all comment. If I drop something in the tutorial class, at least three people collide with each other in their efforts to help me to regain possession of my property. It is all most soothing.

After the exams, of course, the trouble starts—the letters from Mum and Dad, the interviews, the postmortems, the medical certificates, the tales of horrifying mischance, the fatherly advice, the promises of reform, the choice of alternative careers. But by then I have had my fortnight, and fate cannot touch me.

Letters to the Editor

LABELLING OF MEDICINES

SIR,—The question in the House of Lords by Lord Archibald on May 2 arising out of the recent recommendation of the Joint Formulary Committee draws attention again to the highly unsatisfactory position regarding the labelling of medicines. Previously it had usually been possible to ensure that the name of the preparation was written on the container simply by adding the letters N.P. to the prescription. The decision of the Joint Formulary Committee, not unanimous as evident from my letter, now means that if a doctor wishes the name of the drug to appear he has to write out his prescription almost in duplicate. It is easy to predict that this clumsy method will hardly ever be employed and with the abandonment of the N.P. convention the names of drugs will now appear even less frequently on the container.

In my experience much opposition to labelling with the name of the drug comes from pharmacists, but I doubt if they appreciate fully the increasing difficulties of the present situation. I encounter the problem chiefly in the medical outpatient department and in dealing with emergency admissions. A majority of patients referred for consultant opinion nowadays state in their history that they are taking some drugs. The referring letter only occasionally mentions this, but often the patient, hoping to be helpful, brings them to the clinic. One can be certain that the superimposed label on the container will not give much assistance, but sometimes this may be removed and the manufacturer's label found intact underneath. More often a guess has to be attempted, though identification may be possible after expenditure of time with the hospital pharmicist and his charts. Even after telephoning the doctor the mystery may not be solved, as sometimes he cannot remember and has no record. With the advent of the holiday season, movement of patients and employment of locums the position becomes even more difficult. Yet information on this point is very important because drug therapy often seriously confuses the interpretation of clinical and laboratory findings and diagnostic errors on this account are not uncommon. I have on several occasions seen patients admitted to hospital and subjected to extensive and expensive investigations solely through ignorance of the medication that has been prescribed. The importance of knowing what may have been taken by or prescribed for a patient admitted as an emergency needs no emphasis.

The difficulties are by no means confined to hospital practice. Partners, doctors on call at weekends, assistants, and locums are often unaware of what their colleagues have prescribed and do not have the information at hand when called to advise the patient. Confusion may also arise with patients sent home from hospital with drugs if the discharge letter is not immediately available. Clearly the position could be improved a little if fuller information were exchanged between doctors; but in practice, even with more foresight, the doctor would frequently still be confronted with a patient and a box of unknown tablets. Good medicine cannot be practised nowadays in ignorance of the drugs that a patient has been taking.

I am fully aware of the many theoretical arguments that have been put forward against the inclusion of the name of the drug on the label but am unaware of any reliable evidence that they apply at all frequently in practice. The necessity for the present omission of information should be fully justified in view of the confusion that it causes. It is only rarely advisable to conceal the nature of a treatment from a patient, as witnessed by the fact that prescriptions are practically never placed in sealed envelopes. It is thus open to the patient to attempt to decipher what he is going to receive.

The introduction of many potent drugs during the past twenty-five years has tremendously changed the practice of medicine and in my opinion it is no longer justifiable to continue our present outmoded system of labelling medicines. The name of the drug should be shown on the container unless the doctor orders otherwise.

Department of Pharmacology
and Therapeutics,
University of Sheffield. G. M. WILSON.

SELECTION BY INTERVIEW

SIR,—As members of a course for physician superintendents, we have had occasion, with the help of a management consultant to industry, to examine the principles of staff selection. Although procedures differ from place to place, and according to the status of the medical candidates, none of us (and our joint experience of psychiatric hospitals totals 150 doctor-years) has encountered anything to match the techniques which business houses are being advised to use. The financial survival of these concerns depends upon choosing the best candidate and placing the right man in the right job. The following points merit careful thought:

(1) Selection committees should consist of not more than four or five people, each with special knowledge of some aspect of the job in question.

(2) The members of these committees should be thoroughly acquainted with the situation and kind of duties which the candidate will carry out, and with the people with whom he will work. Lack of success by interviewers is usually due to absence of this "general preparation". (We know, for example, that committee members do not always visit the hospital for which they are selecting a consultant.)

(3) The setting of the interview should be informal and, so far as possible, relaxed.

(4) Candidates for senior appointments should never fail to visit the place where they will work and talk to the other senior staff (in hospitals the medical, nursing, and administrative officers). The views of these people on the spot as to which candidate is likely to fit in best should then be given due weight.

(5) Waiting time before the interview should be about 5 minutes—to allow the candidate to compose himself. An appointment system is essential.

Some of the present selection procedures do not appear to follow these precepts.

ROSALIND I. BEARCROFT
RICHARD FOX
A. N. GRAHAM
S. C. MACMILLAN
JAMES R. MATHERS
R. MCDONALD
A. MORRISON
J. GORDON RUSSELL
THEO. SCHLICHT
ROBERT H. F. SMITH
E. L. SUTHERLAND
ROBIN WORTERS.
London, W.2.

PSYCHIATRY, THE LAW, AND THE PUBLIC

SIR,—Your report (May 13) of the conference on this subject prompts me to draw attention to a serious deficiency in communication affecting the wellbeing of the children of mentally ill patients.

When I recently discussed the problems of residential and foster-home care for such children with a group of child-care officers and administrators, I found that they had often received little or no information of the impending discharge from hospital and the state of mind of a mentally sick mother whose children had been placed in temporary care. Unexpected and ill-advised visits by the patient sometimes led in these circumstances to avoidable upset of her child, and it disturbed other children and members of the staff also.

Evidently there is a need in some areas for better communication between the psychiatric departments of hospitals and aftercare services on the one hand, and children's departments on the other. Local authorities are now developing their community care of the mentally ill: let us hope that they will ensure easy and regular interchange of information between the respective departments where the interests of children are concerned. Two obvious measures are: (1) that adequate notice should be given to the children's department when a woman who has been mentally ill, and whose child has therefore been in public care, is about to leave hospital, and (2) that a mother who leaves hospital before her mental health is fully restored or who may relapse soon, should be strongly advised by her psychiatrists not to ask for her children to return home until it is clear after a trial period that she is well enough to care for them. In certain circumstances, this may apply to mentally sick fathers also.

Now that early discharge from hospital is so much commoner the risks to a child's emotional stability from the return home of a still-disturbed parent need to be weighed and whenever possible forestalled.

London, S.W.13. HILDA LEWIS.

EFFECTS OF CHLORDIAZEPOXIDE

SIR,—I was interested to read Dr. Sylvester's letter (May 6) in which he mentions that in some children suffering from cerebral palsy, whom he treated with chlordiazepoxide because of its muscle-relaxant properties, he observed increased activity and boisterousness. I have found similar responses in a controlled trial of this drug in children attending a child-guidance clinic; and though the results are incomplete they are worth commenting on, since they suggest that the drug is contra-indicated in certain disorders.

In those conditions where aggressive impulses are already being translated too freely into action, as in brain-damaged children, hyperactive impulsive-behaviour disorders, overt rebellion and delinquency, or the "spoiled child" who reacts with violent tempers to frustration, chlordiazepoxide can sometimes increase the acting-out of emotional drives to a socially undesirable degree. In outpatient practice the drug seems less often suitable for children suffering from behaviour disorders, as the term is usually understood, than the phenothiazine or amphetamine derivatives.

The drug is, however, proving of unique value in forms of neurotic disorder associated with covert or repressed hostility and aggression—e.g., so-called "school phobia" and other forms of separation anxiety due to repressed hostility to a parent, anxiety, phobic, and obsessional states, learning difficulty due to "passive rebellion" against parental pressure, timid children who fear violence and are unable to mix, and paranoid, masochistic children who attract bullying. On chlordiazepoxide most children of this sort show a dramatic change in the direction of confidence, independence, and assertiveness which often persists if the drug is withdrawn after being given for a few months. Though the children frequently become more boisterous and mischievous, teachers and others in charge of them have usually welcomed the change to a more normal, if less "perfect", type of behaviour.

The parents sometimes find these changes difficult to accept, since they usually have similar problems in dealing with aggressive feeling, but it is interesting that many of them, when given chlordiazepoxide, lose their fear of their own anger and find themselves able to meet their children's increased assertiveness with good-humoured firmness and control.

My own impression, from observing changes in behaviour and from the subject's accounts of changes in their feelings and fantasy life, is that chlordiazepoxide may reduce the hostile and aggressive feelings to a point where they are no longer felt as a serious danger and so can be accepted back into awareness or expressed. This would be consistent with the "taming" effect demonstrated in animals. Though it may seem contradicted by the more seriously antisocial behaviour of some children given the drug, in the children concerned covert hostility (in the sense of provocation, spitefulness, and malicious damage) was in fact greatly diminished, even though overt aggression was increased.

The dosage has been 5 mg. twice a day for children of three to five years, and 10 mg. twice a day, increased as necessary to 20 or even 30 mg. twice a day, for older children. No side-effects were noted apart from drowsiness or slight ataxia with high doses.

London, W.1. A. C. R. SKYNNER.

TRISOMIC CHILD OF A HYPERTHYROID MOTHER

SIR,—Dr. van Wijck et al. (April 22) said that they had "failed to find any data in the literature on the incidence of congenital defects in the children of thyrotoxic mothers, such as are described for myxœdematous women".

A paper[1] entitled "Studies of children born to women with thyroid disease" is of interest. The authors state: "Observations of the offspring of hyperthyroid mothers have indicated that such infants were physically normal and that defective features were infrequent, suggesting that excessive transfer of thyroid hormone from mother to fœtus across the placenta either does not occur or does not produce injurious effects." A number of references are cited in support of this statement.

Memorial Hospital of Long Beach, Long Beach, California. GEORGE X. TRIMBLE.

PROTEIN-LOSING GASTROENTEROPATHY IN CONGESTIVE HEART-FAILURE

SIR,—In their paper (April 29) on intestinal protein loss in 3 patients with constrictive pericarditis and 1 with an atrial septal defect, Dr. Davidson and his coworkers discuss whether the possible mechanism for this abnormal loss involves a high venous pressure or some disturbance of the intestinal lymphatic apparatus. We have recently completed a study of albumin turnover and intestinal loss of protein in 3 patients with constrictive pericarditis, which seems to indicate that congestive failure or a raised venous pressure can be ruled out as causative factors.

VENOUS PRESSURE, SERUM-ALBUMIN, AND GASTROINTESTINAL PROTEIN LOSS IN 3 PATIENTS WITH CONSTRICTIVE PERICARDITIS

Patient no.	Sex	Age (yr.)	Venous pressure (mm. saline)	Serum-albumin (g. per 100 ml.)	Fæcal excretion of ^{131}I (%)	
					After ^{131}I-albumin	After ^{131}I-polyvidone
1	M	62	280	4·1	..	0·38
2	M	54	300	1·6	1·12	5·27
3	M	48	127	1·3	1·92	9·23
Normal values		..	<150	4·1–4·9	0–0·39[2]	0·09–1·01

Patients 1 and 2 have had œdema and ascites for several years. Both had a very high venous pressure. Patient 1 has a normal serum-albumin and no evidence of abnormal intestinal protein loss. Patient 2 had a low serum-albumin, a degradation rate of ^{131}I-labelled serum-albumin over three times the normal average, and increased excretion-rates of ^{131}I after intravenous administration of labelled polyvidone and albumin. Patient 3 had suffered from constrictive pericarditis since 1936. Pericardiectomy was performed in 1954, and congestive failure completely relieved. Since June 1960 œdema had reappeared, and was resistant to conventional diuretics. Physical examination revealed no signs of recurrent constriction, and venous pressure in the left jugular vein was normal. Serum-albumin

1. Man, E. B., Shaver, B. A., Jr., Cooke, R. E. *Amer. J. Obstet. Gynec.* 1958, **75**, 728.
2. Schwartz, M., Jarnum, S. *Dan. med. Bull.* 1961, **8**, 1.

was 1·3 g. per 100 ml. The degradation-rate of serum-albumin was 3 times the normal average, and the ^{131}I-polyvidone excretion in fæces was 9·2%.

It appears from these figures that the low serum-albumin and increased intestinal loss of protein in patients with constrictive pericarditis is not dependent on the presence of congestive heart-failure.

Besides the evidence adduced by Dr. Davidson and his co-authors for a disorder of the lymphatic system in these patients, we should like to draw attention to the possibility of an obstructive lesion of the mediastinal lymphatic channels, caused by an inflammatory process in the pericardium and surrounding structures.

Medical Department, Sønderbro Hospital, Copenhagen. KAI HØEDT.
First University Medical Clinic, Kommunehospitalet, Aarhus. VILLY POSBORG PETERSEN.
Medical Department F, Copenhagen County Hospital, Glostrup. MICHAEL SCHWARTZ.

ANAEROBES IN TOW AND WOOL

SIR,—The Ministry of Health drew attention in circular HM (59) 53 of April, 1959, to the contamination of unbleached cotton-wool with tetanus organisms, and recommended that it should not be used in hospital at all.

After this circular was issued Dr. J. Ward, of our department of pathology, examined a sample of tow and found organisms similar to those listed by Dr. Towers (May 6). It seemed logical to us in this group to ban the use of tow as well as unbleached wool from then on.

Since then the manufacturers have been able to supply both tow and unbleached wool sterilised. The rolls of these dressings are very tightly packed; and it would be interesting to have confirmation that steam does in fact penetrate to the centre of the rolls during sterilisation.

North Lonsdale Hospital, Barrow-in-Furness, Lancashire. R. I. DIXON
A. K. MCIVER.

SKELETAL FLUOROSIS

SIR,—On p. 1056 of *The Lancet* of May 13 you reproduced a photograph of apparently stained and mottled teeth classified by Dean as " mild fluorosis ". If this was representative of teeth that might be found in an area where fluoride occurred at the 1 part per million level it is quite obvious that nobody would consider the artificial fluoridation of water.

But Dean's classifications cover the whole range of fluorosis from fine white tracery to virtual tooth destruction, and his categories are correspondingly broad. Where very few cases are reported in the " mild " category, it is to be expected that these were at the lower end of the category, and would be free of such discoloration. I would suggest that this is the explanation of the discrepancy between the photograph and the fact that Galagan and Lamson held that fluoridation at 1 part per million was not objectionable in temperate zones. It seems surprising that Dr. Holman did not ask himself how the public-health authorities in this and other countries could also have held views similar to those of Galagan and Lamson.

Ast et al.,[1] reporting the work of Russell in Newburgh and Kingston, after Newburgh's water had been fluoridated at 1 part per million for ten years, state that 6 out of 436 children were found to have " mild " fluorosis, and in describing this and the milder grades say " the involvement consists of slight whitish flecks or opaque areas on the surface of the enamel without any breaks in surface continuity, excessive wear, *or staining* (italics mine)... a trained eye is required to detect these stages of mottling...". It follows that they did not encounter anything of the sort shown in this photograph.

I have myself examined large numbers of children in high and low fluoride areas of England [2] and the United States, and I have not yet seen any child demonstrating such a degree of dental fluorosis at the 1 part per million fluoride level. Such a condition is rare even at the 2 parts per million level.

Royal Dental Hospital of London, School of Dental Surgery, London, W.C.2. P. M. C. JAMES.

AN ADVERTISEMENT

SIR,—In last week's *Lancet* Dr. Elmes writes condemning this firm's advertisement of the preparation ' Elestol ' in journals issued to general practitioners as dangerous and unethical because the preparation is described as containing " chloroquine phosphate and symptomatic components ".

Dr. Elmes is entirely wrong in alleging that the policy of this firm is to advertise a product with undisclosed components in medical journals. The fact is that the advertisement to which he refers appeared only in *Monthly Index of Medical Specialities*. This publication is accepted by the profession as an excellent price list and reference journal and is in no sense a clinical journal. In every other medical journal carrying this advertisement the component drugs of elestol were given in full.

He further states that in folders sent to practitioners it is possible to discover that elestol contains sufficient prednisone to give 4 mg. per day at the recommended dose as well as 1·2 g. (grains 20) of aspirin in addition to the 0·24 g. chloroquine diphosphate (' Resochin '). In these folders it is clearly stated that the prednisone content, although not high, should not be given in cases with concomitant peptic ulceration, psychoses, and other conditions in which prednisone is contraindicated.

The advertisement clearly states that elestol is a precursor of long-term remission. In other words it gives symptomatic relief during the latent period of between one and three months during which the effect of chloroquine phosphate is slow and disappointing. Clinical trials indicate that this period is usually about 6–8 weeks. It is specifically stated in the folders that elestol should be given only during this latent period. Thereafter, the patient should be switched to chloroquine diphosphate, the recommended dose being 250 mg. daily.

Freedman and Steinberg [3] state that 200 mg. of the sulphate (equivalent to 250 mg. of the diphosphate) twice daily did not give rise to any irreversible toxic effects in 53 patients. Hobbs et al.[4] noted retinopathy only after two years' treatment. Popert et al.[5] confirm Freedman and Steinberg's findings and state that in their experience retinal damage, although requiring further investigation, seems unlikely if the dose of chloroquine does not exceed 250 mg. of the diphosphate daily.

Dr. Elmes's letter is misleading in the extreme and his views quite contrary to the accepted fact of the value of chloroquine diphosphate in the treatment of the most distressing condition rheumatoid arthritis.

Finally, it must be emphasised that 250 mg. chloroquine diphosphate daily is slightly less than one *B.P.* dose.

DONALD WHITFIELD
Medical Service Division,
F.B.A. Pharmaceuticals, Ltd.
London, W.C.1.

SIR,—Dr. Elmes's letter regarding the disclosure of the formula of ' Elestol ' fails to appreciate the purpose and information provided by *Monthly Index of Medical Specialities* (MIMS) for the prescribing doctor.

1. *J. Amer. dent. Ass.* 1956, **52**, 314.
2. *Brit. dent. J.* 1961, **110**, 165.
3. Freedman, A., Steinberg, V. L. *Ann. rheum. Dis.* 1960, **19**, 243.
4. Hobbs, H. E., Sorsby, A., Freedman, A. *Lancet*, 1959, ii, 478.
5. Popert, A. J., Meijers, K. A. E., Sharp, J., Beir, F. *Ann. rheum. Dis.* 1961, **20**, 18.

In the April and succeeding issues of MIMS the full formula, as supplied by the manufacturers, is clearly stated; and, under contraindications, "As for long-term cortisone therapy" is printed in italics to draw attention to these.

Doctors using MIMS are fully aware that all such information can be found in the general index of the journal, and in the May issue the advertisers of elestol, realising this, deliberately arranged that their advertisement should appear on the same page as that on which the full information is given about their preparation.

STUART PHILLIPS
Editor,
Monthly Index of Medical Specialities.
London, W.C.2.

HUMAN RELATIONS IN HOSPITAL

SIR,—Dr. MacSorley (April 29) has done well to draw attention to the need for "consumer satisfaction" in hospitals. Organisation might well improve human relationships as he suggests, but first there must be greater willingness to be organised.

"Organisation and Method" could do much to avoid wastage of time, and time so saved could be spent on being polite. Haste and familiarity are the two most powerful factors in causing hospital staff to treat patients and their visitors as something less than human beings. True, it is difficult at times to be polite when the next job is clamouring to be done, and staff may appear to be callous because they are accustomed to things with which patients are unfamiliar. It is easy to forget that patients may even be a little frightened.

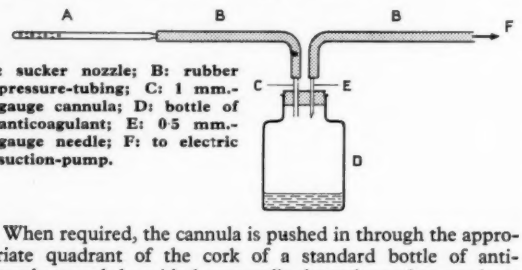
The introduction of a diploma in hospital administration is a progressive step, but the best results will not be achieved until the three constituents of the hospital team—administrators, medicals, and nurses—abandon attitudes of mutual suspicion and criticism and consciously seek to agree and cooperate.

South London Hospital
for Women and Children,
London, S.W.4.
ANNE GIBSON.

AUTOTRANSFUSION COLLECTION SET

SIR,—For the past two years we have been using in this hospital a simple method of collecting blood in suitable cases from the peritoneal cavity, or sometimes the pleural cavity, for autotransfusion.

A sucker nozzle is connected by 4 ft. of rubber pressure-tubing to a 1 mm.-gauge cannula. A further 4 ft. of rubber tubing is connected at one end to a wide-bore (0·5 mm.) needle, and at the other to an electric suction-pump. The whole apparatus, sterilised by autoclaving, is kept in a tin.



A: sucker nozzle; B: rubber pressure-tubing; C: 1 mm.-gauge cannula; D: bottle of anticoagulant; E: 0·5 mm.-gauge needle; F: to electric suction-pump.

When required, the cannula is pushed in through the appropriate quadrant of the cork of a standard bottle of anticoagulant, and the wide-bore needle through another quadrant of the same cork. The free end of the rubber tube is connected to an electric suction-pump; and when it is switched on, blood is readily drawn into the bottle. This process can be repeated, and several pints of blood thus collected for transfusion. Up to 4 pints have been collected by this method, and successfully transfused.

Small blood-clots are occasionally sucked into the bottle, but the filter on the blood-giving set prevents their transfusion into the patient. The sucker nozzle needs a rinse through from time to time; if the cannula becomes blocked a sterile trocar may be passed through it.

General Hospital,
Ijebu-Ode, Western Nigeria. G. I. B. DA COSTA.

PAVLOV OR FREUD?

SIR,—Your leader of March 4 and the discussion of the treatment of transvestism often mentioned the aversion treatment of alcohol addiction. Successful treatment (by any method) of the "symptom" of alcoholism seems indeed often to be followed by an all-round improvement extending to other spheres of the alcoholic's behaviour. Furthermore, "symptom substitution" in these people seems uncommon, apart from the not infrequent substitution of drug habituation for alcoholism. As for results of treatment, however, there is no evidence that aversion therapy is superior to other methods.

It is extremely difficult to compare the results with various methods obtained by different therapists, because in alcoholism the therapist's attitude towards the patient often seems more important than the method he uses; furthermore, the results must depend to a large extent on the type of patient. Thus Lemere, Voegtlin, and their coworkers, pioneers in the conditioned-reflex treatment of alcoholism, state that inadequate and psychopathic alcoholics do not often respond [1] and that "the type of patient best suited [to this treatment] . . . is the essentially normal, stable person who has gradually developed a habit until it has got the best of him and now he wants help in breaking the habit and is willing to stop drinking for good".[2] This is, of course, the type of alcoholic who may be expected to do fairly well with any other method. Wallerstein and his coworkers [3] who compared different treatment methods carried out under comparable conditions found the results of aversion therapy to be less good than those of other methods.

In trying to evaluate aversion treatment of alcoholism several other considerations must be kept in mind. Thus, with apomorphine, Dent believes that aversion is not the main factor.[4] Other authors too feel that other forces are of considerable importance in "aversion" therapy.[5 6] Then again, this form of treatment is often combined with other methods.[7] It has also been stated that many workers using conditioning treatment for alcoholism have failed to adopt sufficiently rigorous procedures.[8 9]

The approach of Alcoholics Anonymous, who concentrate primarily on alcoholism as the "disease" itself without regard for underlying causes, has in practice often proved very successful. It is probably true to say that psychiatrists often fail with alcoholics because they tend to neglect the importance of the drinking problem itself and concentrate exclusively on dealing with the underlying causes. But it seems unlikely a priori that in a condition as complex as alcoholism one type of therapy should invariably be the best in every single case.

There are many different types of alcoholism: as Jellinek has recently put it alcoholism is a branch "genus" comprising many "species".[10] Among them is, for example, Jellinek's "alpha alcoholism", a ". . . purely psychological continual dependence or reliance upon the effect of alcohol to relieve bodily or emotional pain".[11] It seems unlikely that in such a case therapy directed at the drinking problem alone without regard to underlying conditions should prove sufficient. In the relatively stable alcoholic personality types "symptomatic" treatment may indeed often be enough to produce an all-round improvement; but in the more unstable and neurotic personalities attention to underlying conditions seems to be needed *in addition to* more direct attempts to encourage the alcoholic to give up drinking. In hospital practice the more neurotic personality types of alcoholics predominate, and whereas in

1. Voegtlin, W. L., Lemere, F. *Quart. J. Stud. Alc.* 1950, **11**, 199.
2. Lemere, F., Voegtlin, W. L., Broz, W. R., O'Hollaren, P. *Northw. Med., Seattle*, 1942, **41**, 88.
3. Wallerstein, R. S., Chotlos, K. W., Friend, M. B., Hammersley, D. W., Perlswig, E. A., Winship, G. W. Hospital Treatment of Alcoholism. London, 1957.
4. Dent, J. Y. Anxiety and its Treatment. Belfast, 1947.
5. Williams, L. Alcoholism. Edinburgh, 1956.
6. Solms, H. *26 Int. Congr. Alcohol.* Stockholm, 1960.
7. Thimann, J. *ibid.*
8. Eysenck, H. J. *J. ment. Sci.* 1959, **105**, 61.
9. Franks, C. M. *ibid.* 1958, **104**, 14.
10. *Lancet*, March 25, 1961, p. 651.
11. Jellinek, E. M. The Disease Concept of Alcoholism. New Haven, 1960.

our experience conditioned-reflex therapy in fact commonly produced an aversion it was short-lived and in itself not sufficient to prevent these people from resuming drinking. As a general rule it appears that in alcoholics it is just as dangerous to neglect the pre-alcoholic personality factors altogether as to concentrate one's whole interest on them to the exclusion of the drinking history and drinking behaviour.

Rather than approaching an individual case with preconceived ideas (" Pavlov or Freud ") one should aim at evaluating the factors of importance in each case and choose the treatment accordingly: rather than a single method, this will often turn out to be a combination of several therapeutic techniques. The latter should be of sufficient flexibility and range to be adjusted to the varying needs of patients. A therapeutic " cap " should be chosen to fit the individual patient. Therapeutically, alcoholism can be approached simultaneously [12] as a " disease " in its own right—as suggested by Alcoholics Anonymous, with therapy aimed directly at combating drinking, such as aversion treatment or disulfiram—and as a manifestation of underlying personality difficulties.

The example of alcoholism thus seems to support the views of Dr. Bower (April 1) on the advisability of comprehensive treatment, and Dr. MacDonald (April 22) that " . . . behaviour therapists and other psychotherapists could each make contributions to the therapeutic process from seemingly very different points of view ".

St. Bernard's Hospital, Southall, Middlesex. M. M. GLATT.

DIAGNOSIS OF ACUTE APPENDICITIS

SIR,—We have read Mr. Bevan's letter (Feb. 18) and Dr. Crossling's (March 25).

The basis of the cæcal gurgling is fluid accumulated in the region of the ileocolic orifice and the mouth of the vermiform appendix. We have not found that the presence of gurgling excludes a diagnosis of acute appendicitis, presumably because an exudate may be part of the inflammatory process.

St. Josefskrankenhaus, Freiburg im Breisgau, German Federal Republic. H. LEISSNER
NIKOLAUS PAPAGEORGIOU.

INFECTED COCONUT AND PEANUTS

SIR,—We read with interest your annotation of March 25 about infected coconut. The number of salmonella types involved is indeed very large; and we agree that contamination may originate at every stage in the production of this material, which, at least in part, is used for human consumption directly or without sufficient heating.

The difficulties of knowing whether a particular batch of coconut should be condemned or not are clear. But we do not agree that it is a good practice to select the coconut on the basis of the salmonella types present. Basically all salmonellæ are pathogenic to man. Whether a given salmonella type will produce clinical symptoms depends on a combination of factors. For instance, in a weight-reducing product with a coconut basis, a so-called innocent salmonella (*S. waycross*) was isolated by one of us (D.-B.). This type, however, can also cause serious disease in man.[13] This combination of weight-reducing and salmonella contamination may give rise to diarrhœa. It is often hard to detect the routes by which salmonellæ can reach man. We would also stress the shift in relative frequency during the past years of salmonella types isolated from cases of food-poisoning in Western Europe—e.g., the rising frequency of *S. heidelberg*, *S. blockley*, and *S. give*. This is most probably caused by the continual imports of new salmonellæ in fish and animal meal, for example.

Another product imported on a large scale from the tropics is groundnuts. Groundnuts which were brought from Africa to the port of Rotterdam were found to be heavily contaminated. From one sample we isolated *S. dublin*, *S. typhimurium*, *S. urbana*, *S. cubana*, and *S. nyborg*. We cannot yet evaluate the implications of this finding for salmonellosis in man and animals. In fact a groundnut cake imported from Africa (i.e., the residue of the nuts, after removing the oil) was also found to be contaminated. This cake is fed on a large scale to animals.

As with coconut the difficulty lies probably in finding an effective and cheap sterilisation process that does not lower the commercial value of the product. Other workers [14] have also noted salmonella contamination of vegetable-protein products; but we wanted to draw attention to its possible public-health significance.

Municipal Medical and Health Service, Department of Infectious Diseases and Quarantine, Rotterdam, The Netherlands. J. HUISMAN
M. S. M. DANIËLS-BOSMAN.

DELAY IN PUBLICATION

SIR,—As the editor of the *British Heart Journal* I should like to comment on Dr. Wilcken's letter of May 6 concerning the publication of medical articles. The reference to my journal (among others) is clear although it is not named.

The statement is made that British Commonwealth investigators and clinicians of other nationalities who used to publish in British journals are " tending more and more to publish in America ". This statement is at variance with the experience of my journal over the past eight years. During this time publications from the Commonwealth have increased from 6% of our total contributions to 10%; from the U.S.A. the increase has been from 3% to 10½%; from Europe and other countries the increase has been from 3% to 10%. If the *British Heart Journal* were one of several cardiological journals in this country these figures would be striking enough; but these authors knew that it was the only journal, and a quarterly one at that, and I suggest that the facts I have quoted indicate the strong urge that prompts cardiologists all over the world to seek publication in the *British Heart Journal*.

Dr. Wilcken's statement that " the delay in publication averages eleven months; it is now to appear every two months " is inaccurate and out of date. The average interval during 1960 was ten months, and in order to shorten this period an additional number was published in November, 1960, in which the time interval was 8½ months. For the months of January and March, 1961, the interval has fallen from 8¼ months to 6 months. Dr. Wilcken would have written more fairly if he had quoted more up-to-date figures.

I submit, Sir, that important issues in editing are raised by this correspondence. It might be thought from reading it that the shorter the interval the better the journal, but all who have had experience with scientific authors and specialised journals will know that perhaps three-quarters of the contributions need and are benefited by shortening and perhaps recasting. It is this process that makes a time interval of less than five to six months almost unattainable if quality is to be maintained. While I am much concerned to keep the interval to a reasonable minimum I will never allow the character and worth of the *British Heart Journal* to be sacrificed in the interests of rush publication. This practice is likely to mean the acceptance of too many papers as they stand when submitted and without sufficient consideration of their merits.

There is another aspect to this matter. An author whose mind is clear and who writes concisely is likely to produce a paper which immediately commends itself to an editor; the editor is then likely to deal with that paper speedily and before long it is in proof form. Conversely, when a paper is worthy of acceptance but is discursive, repetitive,

12. Glatt, M. M. *Brit. J. Addict.* 1958, **54**, 133.
13. Winkle, S., Rohde, R., Adam, W. *Zbl. Bakt., I Abt. Orig.* 1960, **179**, 584.
14. Haergi, S., Bjovre, H. *Nord. VetMed.* 1958, **10**, 255.

and ill-written the editor naturally cannot feel the same enthusiasm for it.

It is part of the work of an editor to help those contributors who are young or inexperienced or who lack the power to express their thoughts lucidly. Their work may be very well worth publication but the process of putting it into acceptable form, as the result often of a good deal of correspondence, contributes to any delay in publication.

K. SHIRLEY SMITH
Editor, *British Heart Journal*.
London, W.1.

LE FORT'S OPERATION

SIR,—I agree with almost everything which Mr. Wrigley says in the second paragraph of his letter of May 6 but, alas, he has not taken the point I was at great pains to make in my article [1] which perhaps prompted your leader of April 28.

In that article I deplored the fact that elderly women who were considered by their surgeons to be too poor a risk for either a Manchester operation or a vaginal hysterectomy were still being fitted with the Napier pessary or vaginal plugs, and were being doomed to a miserable existence for the rest of their lives, and all this because *their* gynæcologists had not heard of Le Fort, or had given it up because of the bad results which they had obtained.

In some geriatric cases with procidentia of many years' standing, the vaginal walls have large trophic ulcers. These are, in my view, not suitable for any other form of operation. I still think that Le Fort's operation has a very definite, though admittedly limited, place in gynæcology.

C. K. VARTAN.
London, W.1.

SIR,—Although loth to disagree with my former chief and mentor, Mr. Wrigley (May 6), I feel I must support Mr. Vartan and your leader of April 29.

In the same journal in which Mr. Vartan [1] reported 21 cases of the Le Fort operation, I reported 295 such operations performed over a seven-year period.[2] I have since performed another 100 on patients from seventy to ninety years of age.

I agree wholeheartedly that this operation taking less than twenty minutes in most cases and requiring minimal anæsthesia is ideal for the older ladies who are rarely physically fit enough for a Manchester repair. In addition the Le Fort operation is painless, whereas the Manchester repair usually gives considerable discomfort for some time afterwards and often much difficulty with micturition.

Having performed the Le Fort operation regularly for ten years or more, I can report that the results are very satisfactory and the patients are among the most grateful that I have.

EILEEN M. WHAPHAM.
Westcliff-on-Sea, Essex.

CALCIUM DEPRIVATION IN HYPOPARATHYROIDISM

SIR,—Last year [3] we described a sodium-phytate method for diagnosing parathyroid insufficiency. We have confirmed that partial hypoparathyroidism (without tetany) is fairly common. In this area it affects about one quarter of all patients who have had a thyroidectomy.

The symptoms are mostly mental. In a few patients the results of giving phytate were indefinite, despite symptoms which to us suggested parathyroid insufficiency. We are now comparing the results of the phytate test with one described by Kaiser and Ponsold,[4] who gave an intravenous infusion of ethylenediamine-tetra-acetic acid. (E.D.T.A.)

Phytate is now commercially available from Squibb and Sons and from British Drug Houses.

D. B. MORGAN
PAUL FOURMAN
R. H. DAVIS.
Medical Unit, The Royal Infirmary, Cardiff.

1. Vartan, C. K. *J. Obstet. Gynæc. Brit. Commonw.* 1960, **67**, 470.
2. Whapham, E. M. *ibid.* p. 473.
3. Smith, J. W. G., Davis, R. H., Fourman, P. *Lancet*, 1960, ii, 510.

PREMEDICATION WITH ATROPINE BY MOUTH

SIR,—It was refreshing to read the excellent article by Dr. Joseph and Dr. Vale.[5] This is the age of injections; and I feel, as a result, that in anæsthesia at least some of the old arts are in danger of dying out.

If this change contributed to safety one could accept it; but the sight of a small child in the dental chair receiving an intravenous barbiturate—as a recent film advocates—is hardly likely to inspire confidence, at least in the more experienced practitioner. That children, by analogy with adults, prefer a "prick" is just as doubtful. Any opinion which they are capable of expressing is usually coloured by what they have experienced, or been told, beforehand. I believe that one of the hallmarks of a good pædiatric and dental anæsthetist is his ability to "talk down" a child while administering nitrous oxide and oxygen.

For almost thirty years, at this hospital we have given atropine 1 mg. (gr. $^1/_{60}$) by mouth to all children under the age of seven and found it most effective. Dr. Joseph and Dr. Vale are to be congratulated for questioning accepted routine. They have once again proved the wisdom of the advice given by Sir Heneage Ogilvie when asked to suggest a subject for a thesis: "Look around for some subject on which we are all agreed, and start thinking for yourself. You will find you are on virgin ground."[6]

Provided suitable drugs are used, more preoperative medication should be carried out by the oral route.

TOM DINSDALE.
Dental Hospital of Manchester, Manchester.

CHLORDIAZEPOXIDE IN ANGINA PECTORIS

SIR,—We wish to thank Dr. Grant for his comments (Feb. 25) on our paper.[7] We would agree that it is extremely difficult to assess the effect of drugs in angina pectoris. It is possible to have two-thirds of patients claiming substantial benefit from anything they receive during a trial: 13 out of 15 of our patients improved when given the placebo.

To assess whether alleviating an anxiety state might influence these results, we recently ran a short trial of chlordiazepoxide hydrochloride ('Librium'). This drug is stated to have anti-anxiety and tension-relieving effects, and Hirshleifer [8] considered it valuable in angina pectoris.

We gave it to 28 patients with moderate to severe angina pectoris, whose ages ranged from 51 to 71 years (average 62 years). Of these, 14 were classed as having an anxiety state. The dose was 30 mg. per day for a fortnight, increased to 60 mg. per day for a further 2–4 weeks, providing side-effects were absent. According to the criteria previously described,[7] 18 patients were improved. 7 of them volunteered that this was the best tablet they had so far been given for angina.

The side-effects, observed chiefly with doses of 60 mg. per day, were drowsiness in 11 patients, dizziness and staggering in 5, tiredness in 3, impotence in 1, depression in 1, diarrhœa in 1, and indigestion in 1.

The interesting point was that with this drug there seemed to be no correlation between anxiety symptoms

4. Kaiser, W., Ponsold, W. *Klin. Wschr.* 1959, **37**, 1183.
5. Joseph, M. C., Vale, R. J. *Lancet*, 1960, ii, 1060.
6. Ogilvie, M. *ibid.* 1956, i, 115.
7. Murphy, F. M., Barber, J. M., Kilpatrick, S. J. *Lancet*, Jan. 21, 1961, p. 139.
8. Hirshleifer, I. *Curr. ther. Res.* 1950, **2**, 501.

and improvement. We feel that some form of double-blind technique is essential in assessing the effect of drugs in angina pectoris.

Ards Hospital,
Newtownards,
Northern Ireland.

F. M. MURPHY
J. M. BARBER.

SEX-DISTRIBUTION OF MYOCARDIAL INFARCTION

SIR,—In your annotation (Feb. 4) you summarised several large necropsy studies [1–8] from the United States and England in which we observed that in the age-group over 50, the proportions of men and women who died with acute myocardial infarcts were almost identical: 12·5% of the men over 50 years of age examined post-mortem had acute myocardial infarcts, and 12·3% of the women. These observations disturbed us and others since they are quite different from observations based on clinical studies and vital statistics, in which the ratio of men to women dying of acute myocardial infarcts is given variously from 6 to 1, to 3 to 1. In searching for a logical explanation for these apparent discrepancies, we have investigated vital statistics from the United States and have gradually become aware of the remarkable phenomenon of the ratio of *total deaths* in the two sexes.

In all the necropsy series we studied in the United States, we found that in adults the proportion of men to women was approximately 60% to 40%. Our first thought was that consent for necropsies was more easily obtained for men than for women. But analysis of numbers of total deaths (irrespective of whether necropsy was performed) revealed that the proportion of men to women dying in hospitals was also about 60% to 40%, in spite of the fact that approximately equal numbers were admitted for treatment. The next step was to examine the statistics for all deaths in men and women in the urban areas surrounding some of the hospitals. In the first set that we examined (Albany, New York) we found that the proportion of men to women dying in a recent period was approximately 55% to 45%. We then concluded that the predominance of male deaths in the urban population must be balanced by a predominance of female deaths in non-urban areas. Since it is common knowledge that women in general live longer than men, we thought that a preponderance of male deaths in younger and middle-aged groups must be balanced by a preponderance of female deaths in older age-groups. To our surprise, examination of the statistics for the *total deaths* in the United States (urban and rural) for all ages yielded the following results:

*Proportion of total deaths for all ages in the United States 1948-58**

Year	*Male* %	*Female* %
1948	56·9	43·1
1950	56·9	43·1
1952	57·1	42·9
1954	57·2	42·8
1956	57·2	42·8
1958	56·9	43·1

*During this entire period the total number of living women in the population exceeded the number of men. For example, in 1950, there were 99 men for every 100 women and, in 1959, 98 men per 100 women.

On further examination of the figures, the difference in the total number of deaths can largely be accounted for by the striking difference in the death-rates of men and women from 45 to 75. Approximately half the total deaths occur in this age-group and the death-rates of men in this age-group are now almost twice as high as those of women:

Death-rates per 1000 population in the United States in 1959 by sex for specific age-groups

Age-group	*Males*	*Females*
45–54	9·3	4·5
55–64	22·0	10·6
65–74	50·4	29·9

1. Goodale, F., Thomas, W. A., O'Neal, R. N. *Arch. Path., Chicago*, 1960, **69**, 599.
2. Lee, K. T., Thomas, W. A. *Arch. intern. Med.* 1956, **97**, 421.
3. Lee, K. T., Thomas, W. A., *ibid.* 1956, **98**, 80.

These figures for 1959 are quite different from those for 1900:

Death-rates per 1000 population in the United States in 1900 by sex for specific age-groups

Age-group	*Males*	*Females*
45–54	15·5	14·0
55–64	28·5	25·5
65–74	59·1	53·4

It appears that we are passing through a period in which men are not only dying younger but in greater total numbers than women. Thus, even if the percentage of myocardial infarcts among all women dying is similar to the percentage among men (as is the case in the necropsy series we have studied), much fewer women than men will die with myocardial infarcts since fewer women are dying at present.

When viewed in this light, the discrepancy between the necropsy data and the clinical observations is probably more apparent than real.

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F. GOODALE
K. T. LEE
W. A. THOMAS.

PREGNANCY IN A 14-YEAR-OLD MONGOLOID

SIR,—In view of the current interest in mongoloids we would like to report a pregnancy in a fourteen-year-old mongoloid, the earliest such pregnancy reported hitherto, as far as we know.

On Nov. 22, 1960, she gave birth to previable, male twins. The chromosome status of the mother and twins has been investigated by tissue-culture techniques. Chromosome-counts of 47 with XX sex chromosomes and 5 small acrocentric chromosomes have been obtained in cultures of peripheral blood from the mother. Cultures of fœtal blood-cells were also made. These provided chromosome-counts of 46 with XY sex chromosomes. Identity status for the twins is presumptive from the blood-group antigens, haptoglobins, and transferrin types, and from the finding of a monochorionic, diamniotic placenta:

	Blood-groups						*Hapto-globin*	*Trans-ferrin*
Mother	A	CDe/cde	NS/Ns	Le(a−)	Jk(a+)	Kell neg.	1–1	C
Twin A	A	,, ,,	NS/NS	,,	,,	,,	,,	C
Twin B	A	,, ,,	NS/NS	,,	,,	,,	,,	C

Non-mongol status for the twins is supported by the normal chromosome number, and by the opinion of Prof. L. S. Penrose that the palmar and plantar patterns are against mongolism.

To our knowledge there are 9 confirmed cases of mongoloids who became pregnant, and have 11 offspring. Of these, 4 are reported to have been mongoloid [1–4] and 6 (including this set of twins) as non-mongoloid [5–9]; 1 child showed certain features resembling the mongoloid syndrome.[10] This total number of offspring is insufficient for statistical analysis of the incidence of mongoloid against non-mongoloid. However, the findings are not inconsistent with a 50/50 prediction, based on the assumption that mongolism in offspring of mongoloid mothers results from unequal segregation of the three homologous chromosomes during meiosis.

Further details of this case will be reported elsewhere. We wish to thank Professor Penrose for examining the dermal patterns, Dr. Eloise Giblett for providing the blood-group, haptoglobin, and transferrin types, and Dr. Darwin Norby for assistance in

1. LeLong, M., Borniche, P., Kreisler, L., Baudy, R. *Arch. franç. Pédiat.* 1949, **6**, 231.
2. Stiles, K. A. *Proc. 10 Int. Congr. Genet.* 1958, **2**, 276.
3. Rehn, A. T., Thomas, E., Jr. *Amer. J. ment. Defic.* 1957, **62**, 496.
4. Hahnhart, E. *Acta Genet. med., Roma*, 1960, **9**, 112.
5. Sawyer, G. M., Shafter, A. J. *Amer. J. ment. Defic.* 1957, **61**, 793.
6. Levan, A., Hsu, T. C. *Hereditas*, 1959, **45**, 665.
7. Forssman, H., Thysell, T. *Amer. J. ment. Defic.* 1957, **62**, 500.
8. Forssman, H., Lehmann, O., Thysell, T. *ibid.* 1961, **65**, 495.
9. Mullins, D. H., Estrada, W. R., Gready, T. C. *Obstet. and Gynec.* 1960, **15**, 781.
10. Schlaug, R. *Acta genet., Basel*, 1957, **7**, 533.

chromosome-counts. We are indebted for financial support to NIH Grant B-2504 (A), the Washington Association for Retarded Children, and the WARC Guilds.

Rainier School,
Buckley, Washington.

H. C. THULINE
JEAN H. PRIEST.

THE RELATION OF METABOLIC PECULIARITIES OF INFANTS TO DIETARY REQUIREMENTS FOR FAT

SIR,—In a recent investigation into the utilisation of 1-^{14}C sodium acetate, 2-^{14}C sodium pyruvate, and uniformly labelled ^{14}C glucose, at least 10 major differences were observed in the metabolism of infants with kwashiorkor and of normal infants of comparable ages.[1] At the same time, several similarities in metabolism in those with kwashiorkor and in controls were deemed to have extensive practical application in devising diets for preventing kwashiorkor, and possibly other nutritional ailments at the time of weaning, or even 2–3 years thereafter.

These similarities in metabolism included inter alia (1) an incapacity of infants under the age of two years to synthesise cholesterol and glyceride fatty acids to any extent from glucose or pyruvate, and (2) a ready ability to synthesise cholesterol, and glyceride, and phospholipid fatty acids from acetate, this synthesis being much more extensive in those with kwashiorkor than in the controls. These observations indicate that the widely held views [2–5] that carbohydrate is an important precursor of fat do not seem to apply to the human infant under the age of two years.

It has been assumed that the 2-carbon fragment derived from pyruvate possesses the properties and reactivity of active acetate.[6] If glucose and pyruvate were oxidised to active acetate in normal infants and those with kwashiorkor, we would expect that the active acetate thus made available would mingle with the acetate pool and in so doing would contribute to the synthesis of glyceride fatty acid and cholesterol. This occurred to a negligible extent and only in the normal infant. Glucose and pyruvate were oxidised to CO_2 by a pathway yielding no active acetate. This other pathway, we suspect, involves the fixation of CO_2 by malate and triphosphopyridine nucleotide as described by Stern and his colleagues.[7] Recent evidence from slice preparations has still further emphasised the importance of CO_2 fixation via dicarboxylic acids, even in the synthesis of liver glycogen.[8] These investigators stated that when $^{14}CO_2$ or carboxyl-labelled pyruvate was the substrate, no label was incorporated into fatty acids. On the other hand, when 1-^{14}C acetate was administered to normal infants and those with kwashiorkor the label was extensively incorporated into the cholesterol and fatty acids of phospholipids and triglycerides. The peak of specific activity of the $^{14}CO_2$ in the expired air was also rapid (within 5–7 minutes), as compared with a much longer latent period after labelled glucose or pyruvate.[1]

Since neither the normal infant nor the one with kwashiorkor readily synthesises cholesterol or fatty acids from glucose or pyruvate, it follows that both are dependent on dietary fat for rapid synthesis of cholesterol and glyceride and phospholipid fatty acid. In this connection, it is noteworthy that the breast milk of all mammals thus far examined contains liberal amounts of fat—over 20% by weight of the milk in some.[9] Furthermore, if the composition of breast milk of various mammals is compared with the time that it takes to double the birthweight of the corresponding newborn animal,[9] it is found that growth-rate, with few exceptions, becomes a function of the fat content of milk and not of the protein alone.[1] A high lactose content tends to be associated with slow growth. It is estimated that human breast milk contains on an average 3·8% fat, 1·6% protein, and 7% lactose, yielding approximately 50% of calories from fat, 9% from protein, and 41% from lactose.

If the composition of human breast milk is now examined in terms of the infant's metabolsim, it is obvious that the inefficiency of the glucose→pyruvate→active acetate pathway is compensated for by the high fat content of breast milk, the fat eventually supplying acetate for cholesterol and fatty-acid synthesis. The protein requirements of human infants, as assessed from the protein content of human breast milk, are relatively small but nevertheless indispensable. But apart from lactose, breast milk contains a much larger proportion of fat than of protein. This, taken in conjunction with the metabolic peculiarities of the human infant in respect of fat synthesis, emphasises its dependence on an adequate amount of suitable fat in the diet. Experiments conducted on our baboons (unpublished work) more than suggest that synthesis of fatty acids and cholesterol from 2-^{14}C pyruvate is in large measure endocrine-controlled, and not necessarily due to an intrinsic defect in metabolism.

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T. GILLMAN.

Department of Pædiatrics,
Faculty of Medicine,
University of Natal, Durban.

J. SCRAGG.

1. Gillman, J., Gillman, T., Scragg, J., Savage, N., Gilbert, C., Trout, G., Levy, P. *S. Afr. J. Med. Sci.* 1961 (in the press).
2. Lawes, J. B., Gilbert, J. H. *J. Anat., Lond.* 1877, **11**, 577.
3. Masoro, E. J., Chaikoff, I. L., Dauben, W. G. *J. biol. Chem.* 1949, **179**, 1117.
4. Schoenheimer, R., Rittenberg, D. *ibid.* 1936, **114**, 381.
5. Stetten, D., Boxer, G. E. *ibid.* 1944, **155**, 231.
6. Korkes, S., del Campillo, A., Gunsalus, I. C., Ochoa, S. *ibid.* 1951, **193**, 721.
7. Stern, J. R., Ochoa, S., Lynen, F. *Fed. Proc.* 1952, **11**, 293.
8. Landau, B. R., Ashmore, J., Hastings, A. B., Zottio, S. *J. biol. Chem.* 1960, **235**, 1856.
9. Brody, S. Bioenergetics and Growth; p. 847. New York, 1945.

"MONGOLISM"

SIR,—A group of physicians and other medical scientists (April 8) have urged the abandonment of the term "mongolism". In supporting their position, I would unequivocally state that if adequate endocrine therapy is instituted during infancy and maintained through the years of development it is possible to efface the major stigmata of the diagnostic facial features of the mongol.

Benda identified in mongols postmortem changes in the anterior pituitary and thyroid which were unrelated to the mental deficiency and the changes in the cerebrum and spinal cord. But before this we had established that anterior pituitary and thyroid extract and calcium were of benefit to mongols. We believe that this therapy can, chiefly by controlling the hypothyroid state, impede the progress of pathological changes during infancy. Such a conclusion was supported by a comparison of endocrine-treated and non-treated mongols at this hospital.[1]

The hypothyroidism in mongolism is usually due to thyrotropic deficiency; but this does not exclude a coexisting primary hypothyroid state any more than it does in a mentally normal child. As in non-mongolian patients, the functional deficit due to hypothyroidism progresses with age. Under endocrine therapy, the mongol infant's osseous development will progress towards normal, with improvement in the abnormal facies.

I suggest "congenital submental and somal deficiency syndrome" as a possible substitute for the oppressive title "mongolism". The report of Ferguson-Smith and Handmaker [2] impedes the acceptance of "trisomy-21 anomaly" for mongolism.

Hospital for Mentally Retarded,
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CHARLES WILLIAM DUNN.

SIR,—I entirely agree with the letter in your issue of April 8 about the rejection of the term "mongolism". Of the terms proposed, I prefer "Down's anomaly",

1. Dunn, C. W. *Delaware St. med. J.* 1960, **32**, 415.
2. Ferguson-Smith, M. A., Handmaker, S. D. *Lancet*, 1961, i, 638.

because when the chromosomal constitution has been determined the title can be completed in the form, for example, of "Down's 21-triplo anomaly" to designate the chromosome abnormality present.

Bucharest, Rumania. A. CARATZALI.

SHORTAGE OF HOSPITAL STAFF

SIR,—The parliamentary secretary to the Ministry of Health, in her reply to Mr. Hale (reported in your issue of April 1), appears to be completely out of touch with the present-day hospital situation. She said of nursing: "... this is a well-paid job, and the fact that we are recruiting nurses confirms that."

When she referred to a fully qualified nurse she presumably meant a State-registered nurse, who after five years' experience gets a salary of £630, including emoluments. Before the war it was £70 *plus* emoluments. With the present-day cost-of-living so high does this seem such a well-paid job?

The staffing position is such that despite the so-called 44-hour week some nurses are still working 48–50 hours, and their consequent fatigue cannot fail to affect their care of patients. Furthermore, in order to bridge the gap in recruitment, nurses of lower intelligence are being accepted in increasing numbers for a shortened training—to say nothing of nursing auxiliaries, who are often untrained. If recruitment is as satisfactory as Miss Pitt claims, why are hospital wards being closed?

The state of affairs in mental hospitals is fully appreciated by "Two Senior Registrars", whose letter (March 18) Miss Pitt would do well to read.

We should like to answer Mr. Hale's question about responsibility, knowledge, and practical experience. A sister-tutor who has spent three years receiving general training, followed by one year's midwifery training, one year studying a special subject, a variable period as a staff-nurse, and a minimum of two years as ward sister, and who finally has taken a university course (which now lasts two years) commands a maximum basic salary after five years of £925 plus the recent—and paltry—increase of 5% to which Miss Pitt refers. Is mass protest the only language which is understood?

Parents who have spent a lot of money on a good education for their daughters hesitate to allow them to enter a profession where status and salary compare badly with those offered by many other careers. The patient will ultimately suffer if standards of entrants continue to fall.

FOUR SISTER-TUTORS.

SIR,—During the E.M.S. days of Hitler's war some teaching-hospital nurses spent a few months training at peripheral hospitals where they profited by the experience and enjoyed it. I feel that if this arrangement could be made again by the matrons concerned it would help to relieve the effects of the shortage in some areas by spreading our nursing resources more evenly. I wish to add this suggestion to the excellent ones of Mr. Devenish and Dr. Coghill (May 13).

Enfield, Middlesex. C. ALLAN BIRCH.

SHORTAGE OF RADIOGRAPHERS

SIR,—I was surprised at the attitude of Miss Wood (Feb. 11) towards medical laboratory technology.

She writes: "Other girls who were not intelligent enough for a full medical career asked me to suggest other openings in associated professions. This has led to quite able pupils undertaking medical laboratory work . . ."

Miss Wood omits radiographers from her list of associated professions and gives the impression that they are more highly qualified than other medical ancillary staff.

I should like to point out that, after the doctor's, medical laboratory work is now one of the most difficult—i.e., highly qualified—professions in the hospital. The full course takes several years to complete. Apart from this, many scientists in hospital laboratories hold university degrees, and are more highly qualified in their own scientific subject than some doctors are in theirs.

There is a shortage of scientists in all branches of medical work precisely because of this attitude that they are inferior; and this is also reflected in the salaries they receive in the National Health Service.

Salisbury, Southern Rhodesia. A. L. C. HUNT.

NOT FOR SALE

SIR,—In 14 years of general practice I have never failed to obtain immediate admission for a medical or surgical emergency on my simple assurance that it was necessary. Nor would I risk losing the friendship of my consultant colleagues by offering to bribe them with a domiciliary visit. So-called "guineapigs"—those who see the Specialist at his rooms and are then admitted to public beds—get no waiting-list preference: they simply pay not to wait in outpatients. I shall be very surprised if any G.P. in this group (Chelmsford) feels able to contradict me.

Maldon, Essex. D. CARGILL.

BUERGER SYNDROME IN THE ORIENT

SIR,—Recently in the Orient we made observations which enjoin caution in rejecting out of hand the existence of "Buerger's disease" as a distinct entity.[1 2] It can be said that, in Japan and Korea at least, relatively frequent instances of the *Buerger syndrome* occur—occlusive peripheral vascular disease in young male smokers, with, in many cases, involvement of the arms as well as the legs, and no evidence of diabetes, hypercholesterolæmia, or disease of the heart and aorta.

These cases were brought to our attention by Dr. Paul S. Crane, Director of the Presbyterian Medical Center, Chonju, Korea, and were corroborated by both the medical literature and replies to inquiries made to surgeons in Japan. The presumption that in the Orient the clinical and pathological picture is less obscured by a high frequency of atherosclerosis and thromboembolic disease prompted us to study the Buerger syndrome there.

Since early 1957 the Center has admitted 62 patients with the diagnosis of "Buerger's disease". The staff-members consider this only the top of a large iceberg, since many mild cases are seen in outpatients, and not admitted for sympathectomy and/or amputation.

A letter was written to each of the 62 patients, and 28 who responded were studied; we also studied a group of 28 unaffected Korean males for comparison.

All the 62 were men. The group of 28 patients studied included 2 brothers, both with disease of all four extremities. All but 5 of the 28 were farmers or farm labourers, of low social and economic status. Almost all lived in farm villages in the rice-growing area of southwestern Korea. Meat, fish, and eggs were almost totally lacking from the diet, of which the staples were rice, kimchi (highly seasoned pickled cabbage and other vegetables), soya-bean cake, and soya sauce. All were smokers, and most smoked heavily.

In the 28 patients studied at first hand, the disease began in their teens in 2, and before age 35 in most (20).

Age at onset	*No.*	*Age at onset*	*No.*
Under 15	1	30–34	7
15–19	1	35–39	5
20–24	5	40–44	2
25–29	6	45–49	1

1. Wessler, S. *Circulation*, 1961, **23**, 165.
2. *Lancet*, 1960, ii, 969.

In 5 of the 28 the disease began in one arm or both. In most one or both arms were involved. In 11 one radial pulse was absent and in 1, both.

Extent of involvement					
All 4 extremities	11	1 leg, 1 arm	1		
2 legs, 1 arm	4	2 legs	7		
1 leg, 2 arms	1	1 leg	4		

In most (2 exceptions are described below) involvement was limited to the popliteal arteries or lower in the legs, and to the bifurcation of the brachial artery or more distal parts of the arm. No hypertension, diabetes, or evidence of visceral disease was discovered.

Serum-cholesterol and fasting blood-sugar levels did not differ significantly from those in the group for comparison. The electrocardiogram was normal in all.

Twenty-four contrast studies (brachial and femoral arteriograms, and aortograms) were performed in 15 of the patients. In the arms these frequently showed obstruction of the radial and or ulnar arteries with compensatory dilatation of the interosseous artery. The leg arteries, which otherwise appeared smoothly lined, were obstructed in the calf area or lower thigh. Changes suggestive of atheroma were rarely seen.

In 2 patients who had sustained severe trauma to the sacral area there was occlusive disease in the iliac arteries. A remarkable feature was the normal appearance of the arterial tree except at these particular sites. The arms were not involved in these 2 patients, who represent, we suspect, a disorder distinct from that in most of the other patients.

In the clinic and the postmortem room both atherosclerotic manifestations and thromboembolic disease are excessively rare in Korea and Japan, especially in the non-Westernised persons of low social and economic status in whom the Buerger syndrome seems more likely. In the Orient, gangrene is an unusual complication of diabetes mellitus. Phlebothrombosis and postoperative pulmonary embolism rarely occur. The largest recent necropsy experience in Korea, where such examinations are unpopular, is that of the National Medical Center in Seoul. In the 342 necropsies (excluding stillborn infants and Westerners) since the opening of the hospital in December, 1958, no instance of coronary-artery disease has been observed.[3] Aortic atheroma was notably mild. Experience in non-Westernised Japanese is comparable.

Visits to 6 medical centres in Japan revealed that most university surgical services admit 10 to 15 patients with the Buerger syndrome annually. The age, sex, and social and economic status of the patients are essentially the same as in the Korean patients.

Of particular interest are the observations of Dr. K. Ishikawa, a surgeon at Tokyo University. In the past 10 to 15 years, in over 200 cases of the Buerger syndrome, 5 have been studied at a time when the radial artery was tender and the pulse weak or absent. Biopsy at this stage revealed inflammatory change, with "round cells", involving the entire thickness of the vessel. It is said, however, that in any artery which is undergoing thrombosis and organisation of a thrombus such a change is likely.

Thus, in the Orient there appears to be in young males a form of obliterative vascular disease which clinically and epidemiologically (and perhaps histologically) does not have the characteristics of atherosclerosis or multiple embolism. The ætiology and pathogenesis may be complicated. That the essential lesion is an angiitis remains to be proved. Angiitis or not, the pathogenesis is not understood but appears to differ from that of other vascular diseases, particularly atherosclerosis.

The observations in the Orient and comparable studies in the United States will be reported in detail later.

This work was supported by the Tobacco Industry Research Committee, and by the U.S. Public Health Service (H3313).

Department of Medicine,
Johns Hopkins University
School of Medicine,
Baltimore, Maryland.

VICTOR A. MCKUSICK
WILLARD S. HARRIS.

3. Ringsted, J. Personal communication, and communication to 38th Parallel Medical Society, Seoul.

KINKING OF THE INTERNAL CAROTID ARTERY

SIR,—Dr. Metz and his associates in their paper (Feb. 25) refer to our article of 1956.[1]

They write: "It is also noteworthy that 1 of the 2 patients with kinking of the internal carotid artery described . . . had previously had a transient hemiparesis." This statement is not correct: neither of our 2 patients had any cerebrovascular symptoms, though we did have a patient who had a transient hemiparesis with a buckled right common carotid artery.

The George Washington
University Hospital,
Washington, D.C.

IRENE HSU
ALBERT D. KISTIN.

TOXIC REACTIONS TO IRON DEXTRAN

SIR,—The difference of opinion between Dr. Ben-Ishay (March 4) and Dr. Grundlingh and Dr. Sahhar (March 18) is, I believe, more apparent than real.

Dr. Hannah Drukker and I have seen many very severe toxic reactions to iron dextran, of the type described by Ross,[2 3] all, so far as I remember, in a particular ethnic subgroup—i.e., Jews from Kurdistan. Dr. Ben-Ishay's patients may well have come from this group; whereas Dr. Grundlingh and Dr. Sahhar's patients probably do not.

Among these Kurdish Jews, intermarriage of first cousins is common. Cohen et al.[4] investigated some of their hereditary conditions; and Szeinberg et al.[5] found glutathione instability in over 30% of them. Besides iron-dextran reactions, Dr. Drukker and I have observed congenital malformations of the heart; hepatosplenomegaly; a congenital hæmolytic anæmia similar to Cooley anæmia, but not identical; and renal hæmorrhages, often due to nephrolithiasis or renal malformations or both.

Jerusalem,
Israel.

A. YUVAL.

THE ASCHOFF BODY

SIR,—Your annotation (Feb. 11) was an excellent and concise statement of present opinion on this controversial structure.

There is no disagreement with the observations of Murphy[6] that focal lesions of heart-muscle and of endocardial smooth-muscle fibres in rheumatic heart-disease may closely resemble typical Aschoff bodies. Yet most pathologists will agree that Aschoff bodies can and do occur in areas totally devoid of muscle elements. I do not believe it is necessary to explain the development of cardiac failure in acute rheumatic fever on the basis of the development of Aschoff bodies from focal myocardial damage alone. Current detailed biochemical studies of myocardial fibres, coupled with electron-microscopic observations, have convincingly demonstrated that the myocardial fibre is an extremely active cell metabolically. Again, most pathologists have been confronted with the problem of patients dying in heart-failure with large hearts and no demonstrable changes in muscle fibres examined by routine histopathological techniques. An alternative suggestion would be that in acute rheumatic fever a variety of substances, as yet unknown, interfere with the effective functioning of the myocardium so that heart-failure follows. Finally, recent studies in our laboratory, using fluorescent-labelled anti-human cardiac myosin, have shown no evidence of localisation in Aschoff bodies that have been studied in auricular-appendage biopsy specimens. Despite the magnificent colour photographs in Murphy's monograph, to which you refer, which are interpreted to indicate that all Aschoff bodies are derived from damaged muscle, a considerable body of evidence is available to refute this concept. Your annotation listed some of this evidence

1. Hsu, I., Kistin, A. D. *Arch. intern. Med.* 1956, **98**, 712.
2. Ross, I. P. *Lancet*, 1955, i, 51.
3. Ross, I. P. *ibid.* 1957, ii, 77.
4. Cohen, T., Goldschmidt, E., Adam, A., Matoth, Y., Theodor, E., Szabo, M. A. *Harefuah*, 1959, **57**, 233.
5. Szeinberg, A., Sheba, C., Adam, A., Ramot, B. *Acta Genet. med., Roma*, 1959, **8**, suppl. 2, 151.
6. Murphy, G. E. *Medicine*, 1960, **39**, 289.

quite well; and I think that the nature of the Aschoff body continues to be a most controversial subject awaiting more intensive research.

Department of Pathology,
New York Medical College,
New York 29, N.Y.

BERNARD M. WAGNER.

USELESS QUARANTINE ?

SIR,—I was glad to read the letters from Colonel Foster (April 1) and Dr. Warin (April 29) deprecating quarantine for the contacts of the common infectious fevers. I would like to go further and abandon isolation even for the *patients* with the four common virus infections—measles, rubella, varicella, and mumps.

In our densely populated communities it is all but certain that, in time, everybody will contract these diseases. It follows that our isolation and quarantine procedures do not succeed in preventing infection of the uncontaminated; they merely delay it. What is the virtue in that ? Delay means that, instead of these annoying but harmless illnesses being contracted in childhood, when they would not matter, they are caught in later school life or even in adult life, when training or work is seriously disrupted. In addition, mumps and german measles are especially hazardous to adults, but not to children.

It is true that babies and toddlers suffering from other diseases should be spared the burden of intercurrent infection. This should be done by segregating them from the rest of the community, while the infectious children should not be prevented from handing on their disease to any healthy child in the neighbourhood.

Whipps Cross Hospital,
London, E.11.

E. HINDEN.

INHIBITION OF CHOLESTEROL ATHEROSCLEROSIS BY IMMUNISATION WITH β-LIPOPROTEIN

SIR,—In our preliminary communication [1] we reported that previous cross-species immunisation with β-lipoprotein inhibits the development of experimental atherosclerosis in cholesterol-fed cocks and rabbits. Siegler et al. (Feb. 18) state that they failed to confirm our results.

We reported at the 3rd Inter-European Congress of Cardiology [2] and published in detail [3] the results of repeated and extended experiments, dealing in addition with the specificity and the possible mechanism of the anti-atherogenic effect of our immunisation procedures. Some of these results are summarised in the accompanying table.

GRADE OF ATHEROSCLEROSIS AFTER CHOLESTEROL FEEDING

Species	Grade 0		Grade 1		Grade 2		Grade 3		Total animals	
	C	I	C	I	C	I	C	I	C	I
Rabbits	..	8	2	7	4	1	18	..	24	16
Cocks	..	9	2	7	16	1	12	..	30	17

C = control groups; I = immunised groups; Grade 0 = aortas with no atherosclerotic plaques; Grade 1 = plaques on up to 25% of aortic surface; Grade 2 = plaques on about 25–50% of aortic surface; Grade 3 = plaques on more than 50% of aortic surface.

These data confirm that immunisation with β-lipoprotein has a definite anti-atherogenic effect. Whereas no atherosclerosis of grade 3 developed in the immunised groups, and only a single case of grade 2 was found in both species, in nearly all animals in the control groups atherosclerosis of grades 3 or 2 was observed.

We agree that the discrepancies between our findings and those of Siegler et al. may be due, as they say, to differences in the animal strains, or in the antigens. (We worked mainly with "lop-eared" rabbits which proved very satisfactory for immunological experiments with β-lipoprotein,[4] and with sexually mature male birds.)

In addition, we found it very important to keep the level of plasma-antibody against β-lipoprotein constantly high (titres in excess of 1/10,000) during the whole period of cholesterol feeding; so we gave anamnestic injections of antigen and measured the antibody level regularly.

Siegler et al. do not give any serological data; and we must assume that their immunisation procedure, which followed our schedule, was to some degree effective in producing antibodies against β-lipoprotein; but the antibody level may have proved ineffective in preventing lipid deposition because of the extremely high plasma-cholesterol values, especially in rabbits (post-treatment levels of 2150–2600 mg. per 100 ml.). This may be why immunisation with β-lipoprotein in the investigations of Siegler et al. lacked anti-atherogenic effect.

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S. GERŐ.
J. GERGELY
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Pathological Department,
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S. VIRÁG
K. FARKAS.

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A. CZUPPON.

1. Gerő, S., Gergely, J., Jakab, L. Székely, J., Virág, S., Farkas, K., Czuppon, A. *Lancet*, 1959, ii, 6.
2. Gerő, S. *Proc. 3 Inter. Europ. Congr. Cardiol.* 1960, p. 7.
3. Gerő, S., Farkas, K., Gergely, J., Jakab, L. Székely, J., Virág, S., Czuppon, A. *Orv. Hétil.* 1960, **41**, 1441.
4. Gergely, J., Gerő, S., Jakab, L., Székely, J., Virág, S., Czuppon, A. *Acta Physiol. Hung.* 1961, suppl. 18, p. 104.

PAIN IN POTT'S DISEASE

SIR,—I have observed 2 cases of Pott's disease in which one of the presenting symptoms was throbbing pain, synchronous with cardiac systole, radiating along the lower intercostal spaces on both sides of the body. This pain was felt only in the semirecumbent posture—e.g., when reading propped up in bed. It disappeared on changing to the supine, prone, or erect position, though sudden stress, such as a cough or sneeze, provoked painful cramps in the same spaces, irrespective of posture, suggesting irritation of intercostal nerves.

In both cases radiography revealed caries of lower thoracic centra with a fair-sized cold abscess in the posterior mediastinum; in one case the shadow of the abscess was almost as wide as that of the heart. Apparently, pus bulges behind the left atrium when the subject is semirecumbent and is thrust upon by the contracting heart. In the supine position the pus gravitates more to the sides of vertebral bodies and is not well placed for transmitting the cardiac thrust to the intercostal nerves. In the prone or erect position the heart falls away from the posterior mediastinum and does not press appreciably on the abscess.

Faculty of Medicine,
University of Malaya,
Singapore.

A. MOHIUDDIN.

STOKES-ADAMS ATTACKS TREATED WITH CORTICOTROPHIN

SIR,—We were interested to read the paper of Litchfield et al.[5] We have also tested the effect of corticosteroid therapy in two patients with Stokes-Adams attacks due to total atrioventricular block.

CASE 1.—A woman, aged 77, had been treated in our hospital seven times since 1954 for intermittent, gripping pains in the precordium and throbbing headache. In 1954 electrocardiography showed a 2 : 1 heart-block; but since 1956 a stable, complete atrioventricular block had developed. In March, 1959, she began to have typical Stokes-Adams attacks 15–20 times a day. Adrenaline and ephedrine failed to produce any improvement, and she was given 40 mg. prednisone daily. Since then she has been maintained on weekly doses of 20 units of depot-corticotrophin. Her symptoms have not recurred; but the complete heart-block has persisted.

5. Litchfield, J. W., Manley, K. A., Polak, A. *Lancet*, 1958, i, 935.

CASE 2.—A man of 60 had been treated for diabetes mellitus and heart-failure in our hospital three times in two years. Electrocardiography showed a variable degree of atrio-ventricular block with bundle-branch block. In 1958 he had typical Stokes-Adams attacks, with a frequency of 25–30 attacks a day. On electrocardiography complete atrioventricular block and multifocal ventricular extrasystoles between attacks were recorded. The usual drugs did not help; so he was given 40 mg. prednisone per day. The attacks ceased; and further attacks were prevented by intermittent treatment with prednisone.

It is noteworthy that in both cases the disease was due to atherosclerosis. Joossens et al.[6] have also reported success in treating a similar case. According to them the corticosteroids influenced the sensitivity of the parasympathetic innervation of the myocardium. This is, however, unlikely, because in complete heart-block stimulation of the vagus nerve hardly affects the ventricle.[7] We share the opinion of Litchfield et al. that the explanation of this improvement may be found in some alteration of myocardial metabolism. The evidence demonstrates the need for further trials of corticosteroid therapy in Stokes-Adams attacks.

Postgraduate School of Medicine, Budapest, Hungary. G. RÓNA
D. LEHOCZKY.

NEW TECHNIQUE FOR STUDYING FAT ABSORPTION

SIR,—In their recent letter, Dr. Sturman and Dr. Rosch (April 1) suggest that the measurement of thyroid uptake and urinary output of ^{131}I after feeding labelled triolein is a reliable method for studying lipid absorption from the gut.

We would suggest that the fraction of iodine which has accumulated in the thyroid is unlikely to be a suitable index. The 24-hour thyroid uptake is variable, even in those with no thyroid abnormality, and has a standard deviation of about 25% of the mean value. To measure thyroid uptake in a separate experiment both complicates the test and increases the radiation hazard. Rather than use the urinary excretion to correct for variability in thyroid function, it seems to us preferable to measure the urinary output with thyroid function blocked.

We proposed[8] that the urinary output after feeding ^{131}I-labelled olive oil, after blocking of the thyroid, would serve as a simple screening test of fat absorption. It permits a dose of 1 microcurie. This contrasts with the 50 microcuries given by Sturman and Rosch, a dose which seems high even for their purposes. Thyroid blocking further reduces the radiation dose to the gland.

In our experience, as more cases are studied, the important problem presented by tests of fat absorption without fæcal collection lies in the occasional finding of anomalously high urinary output of ^{131}I in patients with steatorrhœa. Some unstudied variables are the differential segmental absorption of fat, the rates of breakdown of the absorbed labelled fat, and the amounts of label retained in the tissues outside the thyroid. The study of these cases may improve understanding of the basis of the tests, and lead to their improvement.

Department of Surgery, Queen's College, Dundee. W. F. WALKER.
Department of Medicine, Queen's College. W. K. STEWART.
Department of Pathology, Queen's College. H. G. MORGAN.
Regional Physics Department, Eastern Regional Hospital Board (Scotland). J. McKIE.

6. Joossens, J. V., de Witte, P. E., Kasteloot, H. *Acta cardiol., Brux.* 1957, **12**, 661.
7. Raab, W. *Bibl. cardiol., Basle*, 1956, **6**, 65.
8. Walker, W. F., Stewart, W. K., Morgan, H. G., McKie, J. *Brit. med. J.* 1960, i, 1403.

Obituary

CYRIL GRAY IMRIE

M.D., Hon. D.Sc. Western Univ. Ont., F.R.C.P.

Dr. Gray Imrie, honorary consulting physician to the Royal Hospital, Sheffield, died on May 11.

Imrie qualified from the Western University of Ontario in 1911 and soon afterwards became acquainted with J. B. Leathes who was working as a research assistant and lecturer in chemical pathology in Toronto. When Leathes became dean of the Sheffield Medical School, he persuaded Imrie to join the staff of the department of physiology in Sheffield. In the university atmosphere of research and teaching, Imrie developed his interest in the medical aspects of biochemistry, particularly in the endocrine system—an interest which was lifelong. When he transferred to the teaching hospital he was at first a medical registrar and pathologist to the Royal Hospital. Later he was appointed a consultant physician to the hospital. He was elected F.R.C.P. in 1932, and received the honorary degree of D.SC. from his own university in 1948.

C. H. S.-H. writes:

"Imrie's main contribution to the Royal Hospital was undoubtedly that of developing and maintaining a large diabetic clinic at a time when his own health had begun to trouble him. Despite a steady progression towards a state of crippling which would have forced men of lesser strength of purpose to withdraw, Imrie continued his clinical duties, his teaching, and a busy practice. He was a popular teacher, well liked by undergraduates and registrars, and he continued to lecture on endocrine disorders each year until his retirement at the normal age. The discovery of the steroids of the adrenal gland interested him greatly, and having benefited himself from cortisone he did much to encourage the Sheffield centre for the investigation and treatment of the rheumatic diseases. His personal integrity and steadfastness in the face of physical illness made him universally respected by patients and staff alike. His son, a graduate of Sheffield, chose to practise in Canada and thus fulfilled the return journey which Imrie himself never undertook."

Dr. Imrie leaves a widow, a son, and a daughter.

PETER ALFRED GORER

D.Sc. Lond., M.R.C.P., F.R.S.

Dr. P. A. Gorer, who died on May 11, was reader in experimental pathology at Guy's Hospital Medical School.

He was born in 1907, the son of Edgar Gorer, an authority on art, and on leaving Charterhouse he entered Guy's Hospital Medical School in 1924. There he was fortunate in meeting the late Mr. T. J. Evans, a former dean and a biologist with many diversified interests, who had a flair for recognising talent among his students. Later, while working in physiology under Professor Pembrey, Gorer became interested in hibernation and contributed a lengthy article on the subject to *Biological Reviews*. In this comprehensive survey, he first disclosed the promise which he later fulfilled. Gorer had a lifelong interest in natural history—he was a keen ornithologist and fisherman—and it was through the encouragement that he received from these early associations with Evans, Pembrey, and Nicholson that he was led to take up a career in scientific rather than in clinical medicine.

After leaving Guy's in 1933, Gorer joined J. B. S. Haldane at University College, and in the stimulating atmosphere of that department he developed those interests in genetics which later played so large a part in his researches. From University College he was appointed to the staff of the Lister Institute, and it was while he was there that he began the study of the genetic and antigenic basis of tumour transplantation which occupied him almost exclusively for the next twenty-five years.

In 1940, he returned to Guy's as assistant morbid histologist and hæmatologist, and except for a year as visiting scientist at

the Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine, he remained there till his death. During those years, he developed stage by stage the intricate immunological methods that since, both in his hands and in those of others, have contributed so valuably to our knowledge of the mechanism of the acceptance or rejection of normal and tumour transplants. This work has since had an important influence on ideas in this complex field of immunology both in this country and abroad.

Gorer received recognition for his contributions to immunology first when he was awarded the degree of D.SC. of London in 1940, and later when in 1960 he was elected to a fellowship of the Royal Society. In recent years he took part in many international symposia on transplantation and tissue immunity. At these meetings he was widely known and welcomed both for his own scientific contributions and for his lively participation in discussions on the work of others, when he was able to give full play to his ready wit and his great fund of knowledge.

G. P. W. writes:

"At the time of his death, Dr. Gorer was one of the leading figures in immunology. He had applied himself for many years to a particularly difficult branch of the subject—the immunology of transplantable tumours in pure-line strains of mice. Together with some of his younger associates, he had thrown much light on the differing antigenic constitutions of these tumours, and the appearance in some of them of a cellular component that had no place in the normal tissues of the host animal. In view of the present developments in possible viral neoplasms in mice, such findings were clearly of notable significance, and it is sad that Gorer did not live to develop his discoveries more fully. In addition to the need for scrupulously careful immunological analysis, with its many pitfalls, this work required an extensive knowledge of genetics. The foundations of this knowledge Gorer had laid during the time that he was associated with Haldane at University College. In fact, his scientific career illustrates very clearly the often commanding position in research that is gained by an investigator who has mastered two cognate fields of knowledge and sets himself to find and tie the threads that can unite them.

"No account of Gorer would be complete without some mention of the warm personal qualities that endeared him to a wide circle of friends in this country and the United States. These qualities were particularly valued by his immediate colleagues. His arrival in any group, at lunch or tea, was always welcomed, for, irrespective of whether the conversation was grave or gay, he always had some original and often witty contribution to make. Not least will he be missed by his present and past junior colleagues, for they had constant opportunities of working with him day by day and seeing his conceptions progressively materialise. His modesty and kindliness attached him to them all, while his great breadth of knowledge and perspicacity in an intricate field of research won their deep respect.

"Immunology is a science that is now penetrating rapidly into many fields of medicine, and Gorer was among the leaders in this advance. His early death will leave a serious gap in British medical science."

P. B. M. writes:

"Peter Gorer was the world's leading authority on the manifold problems of tumour transplantation and on the serology of the homograft reaction generally. Nearly twenty-five years ago, when only thirty, he published two papers in the *Journal of Pathology and Bacteriology* which laid the foundations of modern research on the immunological genetics of transplantation: he discovered hæmagglutinating antibodies in the blood of mice bearing homografts of tumours, and showed that the power to excite the formation of these antibodies went hand in hand with the properties that called forth resistance to the foreign growth. The combined genetical and immunological analysis of 'histocompatibility genes' and their antigenic products occupied him, and a succession of devoted and highly able pupils, for the rest of his life. He constantly improved the techniques of the hæmagglutination test, and each improvement increased the resolving power of his analysis of the complex H-2 locus; he discovered that some kinds of cells—not only tumour cells—can be destroyed in vitro by the action of cytotoxic antibodies; his latest work, in progress when he died, pointed towards a synergistic action between antibodies and sensitised lymphoid cells. Some of his most penetrating work was done in, or in collaboration with, the great laboratory of mouse genetics at Bar Harbor, Maine.

"Gorer was very much more than a man who made important particular discoveries. He was a master of the arts and theories of transplantation, a man whose opinion everyone sought and paid heed to; he was unique in his combined knowledge of pathology, immunology, and genetics. His style of thought and discourse was witty and forcible. Something of it can be seen in his papers, but it was seen best in conversation at leisure with his colleagues—a mixture of laughter, shrewd judgment, and the excitement of scientific discovery. Being of complete intellectual honesty, Gorer never resented the criticisms of others and caused no resentment in others by his own; he was a well-loved man, and his death at the height of his powers has caused his colleagues great sorrow and dismay."

Dr. Gorer was married twice. His first wife, Gertrude Kahler, died a few years after their wedding. He met his second wife, Elizabeth Bruce Keucher, whom he married in 1947, while he was at Bar Harbor. He is survived by his widow and a young son and daughter.

Parliament

QUESTION TIME

Naming the Fined

Mr. MARCUS LIPTON asked the Minister of Health whether he would publish the names of doctors and dentists who were fined by local health executive councils.—Mr. ENOCH POWELL replied: No, Sir.

Mr. LIPTON: Even if this is about the only official secret which the Government are able to keep, is it not nevertheless a public scandal that doctors and dentists who are paid out of public funds and who let the public down should be covered by this conspiracy of silence? Is he not aware that public opinion is very strongly in favour of these guilty persons being named?—Mr. POWELL: Where it is held by the National Health Service tribunal that, in the public interest, a practitioner should not continue to practise under the health service, then the name is published. But in the cases where the name is withheld, what has happened is that there has been established a breach of contract between the practitioner concerned and the executive council. In a case of that kind it is not the practice that names should be disclosed. Any remedy, either civil or criminal, against the practitioner is unaffected.

Mr. KENNETH ROBINSON: Does not the Minister appreciate that to the public at large it is rather mysterious why a doctor's moral lapses should nearly always obtain the widest publicity whereas professional shortcomings, which may well affect the life or health of a doctor's or dentist's patients, are shrouded in anonymity? Does not he think that the situation might be looked at again?—Mr. POWELL: When matters are brought to light in the course of these disciplinary cases they should be investigated by the General Medical Council or the General Dental Council. They are brought to the attention of these bodies, which are the appropriate ones for that purpose.

Mr. DENIS HOWELL: How can the public be protected? Where do they come in in the Minister's estimation?—Mr. POWELL: If the professions concerned wish to represent to me that names should be published, I will take account of their point of view.

Mr. W. W. HAMILTON: Would the right hon. Gentleman consider the desirability of publishing the names of people who commit a second offence and of making it clear that they are in breach of contract so that, although it is not a criminal offence, the public will be in a position to judge the worth of

their work?—Mr. POWELL: When it is undesirable that a person should continue to provide services in the National Health Service, the name of the practitioner concerned is published and he is taken off the list. Secondly, where it appears prima facie that there are matters which ought to be brought to the attention of the General Medical Council or the General Dental Council they are brought to their attention.

Foot-and-mouth Disease Vaccines

Mr. E. D. L. DU CANN asked the Parliamentary Secretary for Science what reply he had made to the request of the Pirbright Research Institute for a grant of £100,000 for the development of an anti-foot-and-mouth-disease vaccine. Mr. DENZIL FREETH replied: The governing body of the Foot-and-Mouth Disease Research Institute, Pirbright, have been authorised to negotiate an agreement with a pharmaceutical firm, the Wellcome Foundation, Ltd., for the production on a commercial scale at Pirbright of foot-and-mouth vaccines for sale abroad. The cost of the buildings required is estimated to amount to about £100,000, and will be eligible for grant-aid from public funds.

Senior Registrars

Mr. L. A. PAVITT asked the Minister what would be the annual cost of absorbing all-time expired senior registrars into the consultant grade.—Mr. POWELL replied: The initial annual cost would be up to £90,000, depending on whether they elected to be whole-time or otherwise.

Waiting-lists

Mr. PAVITT asked the Minister if he would institute an inquiry into the periods of waiting for hospital beds by patients for whom treatment has been ordered.—Mr. POWELL replied: I am considering what changes are needed in the present system of compiling and analysing waiting-lists to ensure that they are realistic, and what further advice can be given to hospital authorities to assist them in reducing the backlog of cases in the various specialties.

Fall in the Number of Prescriptions

In England and Wales the number of prescriptions dispensed was 23·6 million in January, 22·2 million in February, and 17·5 million in March. The two last figures are provisional.

Waiting-list of Subnormals

On Dec. 31, 1960, in England and Wales 5502 subnormal and severely subnormal people were awaiting admission to hospital.

Distinction Awards

On Dec. 31, 1960, in England and Wales the number of consultants in each specialty receiving a distinction award was as follows:

Specialty	At Dec. 31, 1960				
	Number of consultants	Awards			
		A plus	A	B	C
General medicine	883	18	68	151	270
Diseases of the chest	299	..	14	22	59
Mental health	679	4	5	30	59
Neurology	82	3	9	17	26
Pædiatrics	214	2	13	31	59
Radiology	477	2	9	22	69
Radiotherapy	126	3	4	10	21
Physical medicine	89	..	1	2	11
Pathology	725	7	27	51	101
Infectious diseases	37	..	1	3	13
Dermatology	147	1	4	17	27
Venereology	75	..	..	2	12
Ophthalmology	301	2	13	25	45
General surgery	872	20	49	139	261
Anæsthetics	828	3	6	27	84
Neurosurgery	61	4	5	10	16
Plastic surgery	58	1	1	13	17
Thoracic surgery	93	4	9	21	26
Orthopædic surgery	348	6	14	42	72
Dentistry	264	1	4	13	35
Ear, nose, and throat surgery	308	..	13	29	58
Obstetrics and gynæcology	450	9	18	54	113

Notes and News

SALARIES AT CAMBRIDGE

IN publishing this week an advertisement for a statistician to the Cambridge medical school, we must point out that Cambridge at present differs from other universities in its payment of medical members of the teaching staff. After the report of the Royal Commission last year, the University Grants Committee recommended new differential payments for clinical teachers; but in February the regent house at Cambridge decided that differential payments should no longer be made. This decision has in turn obliged the British Medical Association to say that, as things stand, it cannot advertise appointments in the university, medical or other.

The view which prevailed in the regent house was that "academic life should be a vocation in which adequate provision should be made for its followers to sustain an appropriate standard of life, but without undue reference to levels of remuneration in other fields . . .". This view must command respect, but it would be more impressive if the differences between the incomes (from various sources) of university teachers were not already so considerable. The British Medical Association's decision arises from its policy, laid down in 1956, that "medical men and women in whatever form of medical practice or service they are engaged should be remunerated as doctors". Attractive though a particular university may be, we cannot help feeling anxiety about the prospects of continuing an important medical school—let alone enlarging it as planned—if the remuneration of its teachers is deliberately kept below what is paid to comparable teachers elsewhere.

PRIORITIES IN PRACTICE

IN a review [1] of the development of the welfare services for old people since 1946, Mr. Peter Townsend said that so far as the figures could be interpreted it seemed that last year the gross expenditure on the aged by the home-help, district-nursing, and health-visiting services was £10–11 million. Other local-authority and voluntary expenditure on such services as meals in the home, chiropody, and laundry might bring the total spent on domiciliary services for the aged to rather more than £12 million. Was this, he asked, what we meant by giving priority to the preventive and home services? Was £12 million adequate in relation to the sum being spent on, say, the ambulance services, the care of mothers and young children, or the executive councils' share of superannuation for general practitioners? Was it realistic in a period when there was growing insistence on the quick turnover of geriatric beds and on the importance of avoiding institutionalisation? Many services had scarcely kept pace with the rising numbers of old people, still less met their needs, and despite public advocacy of the principle of maintaining the elderly in their own homes, there was no evidence of the switch in priorities which would be necessary if this principle was to be applied in practice. Mr. Townsend would like to see one department in each local area made responsible for the social and welfare needs of handicapped and aged people living in their own homes. Some people argued that this responsibility should rest with the health department. But his own studies suggested that this was unlikely to be the best solution. In principle it would seem advantageous to make a clearer distinction between the administration of health and welfare services, and he believed there were strong arguments for the enlargement of the local-authority welfare department. It could well be responsible for compiling a list of isolated and homebound people, arranging for them to be visited, and managing the home-help service.

Another way of helping the aged would be to second a district nurse and a health visitor or a psychiatric social worker to a group of general practitioners, who would then aim to examine regularly all their elderly patients over, say, 75 or 80. He doubted whether general practitioners would be able to play a full part in the development of preventive health ser-

1. An address in Bath on May 12 to the Association of Directors of Welfare Services.

vices and aftercare unless there was a deliberate attempt to encourage groups of them to work more often together, with proper help from ancillary workers.

INDUSTRIAL CLINIC FOR SMALL FIRMS

AN industrial health clinic on the Poyle industrial estate, at Colnbrook, Bucks, was opened on Monday by Mr. John Hare, Minister of Labour. It is the first clinic of the Slough industrial health service to be set up outside the Slough trading estate. It will serve the 60 firms on the Poyle estate, several of which employ less than 25 workers. Member firms will pay 10*d.* a week for each employee, and nearly half the companies on the estate with some 1500 employees have joined the scheme.

Mr. Hare said he would like to see many more such schemes set up in all parts of the country. For the larger firm to provide adequate medical supervision for its workers should present no great problems, but for the smaller firm it was not so easy; clearly it would be impossible for every firm to provide its own industrial health service. "The obvious answer for the small firm lies in the group scheme. Unfortunately there are very few such schemes at present."

The new clinic has been built and equipped by a grant from the Nuffield Provincial Hospitals Trust. It is a self-contained unit consisting of a waiting-room, treatment-room, and consulting-room. It is open from 8.30 A.M. to 5.30 P.M. daily, and is equipped to deal, in the first instance, with all cases of injury or illness at work. Experience in fifteen years at Slough has shown that 99% of cases are able to return to work immediately after treatment, and only 1% have to be referred home to their own doctors or to hospital.

The Slough industrial health service, which began in 1947, now includes a central polyclinic, three sub-clinics (including the new one at Poyle), medical departments in the larger firms, and a mobile dressing-station. The laboratories of the occupational hygiene service, which was formed by the industrial health service in 1950, are in a building adjoining the central clinic. This unit is now self-administered, but the facilities for the recognition, evaluation, and control of hazards to health in industry are available to all member firms without charge and to other industrial concerns on a fee-for-service basis.

A COMMUNITY SERVICE AND ITS DIFFICULTIES

PLANS for the expansion of our community services will gain from study of the difficulties met in small progressive outposts of practical experience. A useful report of this kind is Dr. G. P. Egan's account [1] of the efforts of the Liverpool Psychiatric Day Hospital to establish a small occupational unit for male schizophrenics living at home, on the lines of the Bristol Industrial Therapy Organisation.[2]

Dr. Egan explained that in the three and a half years that it had been open the day hospital had accumulated a group of patients whose mental incapacity appeared to be permanent. The family's tolerance to such people dwindled rapidly if they remained at home, idle, and inactive all day. Relatives liked to feel that something, however little, was being done for the patient. They deteriorated, partly from the inactivity and partly from the mounting intolerance, and pressure for admission to hospital followed. Yet at the day hospital their presence was not helpful to the other patients. It was therefore decided to separate them into an independent group, and try to find some work for them. But Dr. Egan and his colleagues were singularly unsuccessful in persuading industrial firms on Merseyside to provide piece-work which could be done in the improvised workshop at the day hospital. Because of this disappointing experience he wondered how successful local authorities would be in running occupational centres and sheltered workshops. The disability of psychiatric patients was of a different quality to that of the blind, deaf, or otherwise physically handicapped, and patients and their relatives rightly expected continuity of psychiatric interest. Yet local-authority services, in Dr. Egan's view, interpreted their obligation to handicapped patients as the provision of "care", which tacitly implied the exclusion of treatment. The Bristol project had been conceived by the fertilising union of psychiatrists interested in "treating" rather than "caring" for their patients, and philanthropic industrialists with a vocation to help the mentally handicapped rather than be politely sympathetic. Some progressive local authorities might find the inspiration to emulate the Bristol work, but the experiment on Merseyside had confirmed that they would face difficulties. He believed that these could be overcome only by enlisting all the resources of the hospital services. He added: "By passing our patients on to the local-authority health services we send them up that blind alley, heretofore called 'After Care' now renamed 'Community Care'."

1. An address to the Liverpool Women's Youth Services Club, April 19, 1961.
2. Early, D. F. *Lancet*, 1960, ii, 754.

INCREASES IN PAY FOR SERVICE MEDICAL OFFICERS

THE Army Council has approved revised rates of pay and additional pay for officers of the Army Medical Services, other than National Service officers. The old and new rates (effective from April 1, 1960) are:

	New £ s	*Old* £ s
Lieutenant	2 3	2 0
Captain		
On appointment	2 9	2 6
After one year	2 11	2 8
,, two years	2 13	2 10
,, three years	2 15	2 12
,, four years	3 2	2 19
,, six years	3 5	3 2
Major		
On appointment	3 18	3 16
After two years	4 4	4 2
,, four years	4 10	4 8
,, six years	4 13	4 11
,, eight years	4 16	4 14
Lieut.-Colonel ..	5 1	4 19
After two years	5 7	5 5
,, four years	5 13	5 11
,, six years	5 16	5 14
Colonel		
On appointment	6 5	6 3
After two years	6 8	6 6
,, four years	6 11	6 9
,, six years	6 14	6 12
Brigadier	7 3	7 1
Major-General ..	9 0	9 0
Lieut.-General ..	11 6	11 6

Junior specialists and senior specialists, if National Service officers in their first 18 months of whole-time service, will receive 6*s.* a day additional pay instead of 2*s.* Senior specialists, including National Service officers, after 18 months' whole-time service, will receive 16*s.* a day additional pay instead of 12*s.*

Similar changes have been agreed for the Royal Navy and the Royal Air Force.

University of Cambridge

On April 29 the following degrees were conferred:

M.D.—R. M. Buckle, J. T. Rowling.
M.Chir.—*I. J. Cour-Palais, J. A. MacDougall, B. A. Maurice.
M.B., B.Chir.—* R. N. Davies.
M.B.—D. R. Bailey, * W. K. Blenkinsopp, Peter Richards.
* By proxy.

University of Melbourne

Dr. E. B. Verney, F.R.S., Shield professor of pharmacology in the University of Cambridge, has accepted a personal chair in the department of physiology at Melbourne, Australia.

Royal College of Surgeons of England

At a meeting of the council on May 11, with Sir Arthur Porritt, the president, in the chair, Dr. E. Rohan Williams was admitted to the fellowship after election. Mr. T. A. Ogilvie was elected to the fellowship *ad eundem*.

The Cartwright prize for 1960 was presented to Prof. G. L. Howe.

Postgraduate diplomas and diplomas of membership were conferred on the candidates named in the report of the comitia of the Royal College of Physicians (*Lancet*, May 6, 1961, p. 1009).

Beit Fellowships

Prof. Alexander Haddow has been elected a member of the advisory board, and the following elections to fellowships have been made:

Junior fellowships.—S. P. R. Rose, B.A. Cantab. (at the department of biochemistry, University of Oxford; R. Laverty, PH.D. N.Z. (at the Agricultural Research Council's Institute for Animal Physiology, Babraham); Ruth F. Itzhaki, PH.D. Lond. (at the department of radiotherapeutics, University of Cambridge); C. W. F. McClare, B.A. Cantab. (at the department of radiotherapeutics, University of Cambridge); S. S. Hayreh, M.B. Punjab (at the Institute of Ophthalmology, London).

Fourth-year fellowship.—Margarethe M. A. Holzbauer-Sharman.

Royal Australasian College of Physicians

The following have been admitted to fellowship:

Under Article 44: Kevin Brennan (Victoria); W. H. Trethowan (New South Wales). *Under Article 42:* P. J. Benjamin, W. J. C. Burke, E. D. Burnard, J. H. Deakin, N. L. Edwards, S. E. J. Robertson, T. I. Robertson, J. N. Sevier (New South Wales); A. J. M. Dobson (Tasmania); J. Etheridge, A. C. Schwieger (Victoria); J. J. Fitzwater (Queensland); C. Cresson, D. S. Malcolm, I. A. M. Prior, A. S. Turner (New Zealand); H. G. Rischbieth (South Australia).

The following have been admitted to membership:

W. Douglas, Ian Ferguson (Queensland); P. A. Castaldi, E. L. Corlette, R. W. Johnston, B. M. Learoyd, B. P. O'Connell, B. McK. Rush, R. R. Taylor, I. L. Thompson (New South Wales); J. P. Carew, J. A. Fuller, June L. Howqua, P. J. Kiernan, A. A. Large, C. R. Lucas, I. G. McDonald, Margery C. McKinnon, Aubrey Pitt, Bernard Sweet, J. R. York (Victoria); J. G. Mortimer (New Zealand); J. H. Allison, J. M. Angeloni, E. R. Beech, Michael Duffus, T. M. Gilbert, R. C. Godfrey, Paul Mestitz, W. G. Smith, J. L. Smyth, Dr. T. Waters (Western Australia).

Training of Surgeons

The council of the Royal College of Surgeons of England has established a post of adviser in surgical training, the first holder of which is Sir Clement Price Thomas. Some of the duties of the adviser were originated by Sir Gordon Gordon-Taylor, and are being continued by Sir Clement; these include advice to young surgeons on their future surgical training.

British Society for Immunology

A meeting of this society will be held from June 1 to 3 at the Middlesex Hospital Medical School, Cleveland Street, London, W.1, starting at 10 A.M. each day. The programme will begin with a symposium, under the chairmanship of Prof. P. C. C. Garnham, on immunity to protozoa.

Diphtheria in South-east London

A boy of 9, a pupil at St. Antony's Roman Catholic School, Lordship Lane, East Dulwich, fell ill on May 1, and investigations indicated that the illness was a "doubtful case" of diphtheria. One of his brothers, who also had not been immunised, was identified as a definite case and two other brothers (one of whom had had primary immunisation) as carriers. Among pupils of the school, two other carriers have been identified in another family, and there are so far known to be five individual carriers among other pupils.

Wandsworth Chest Clinic

On May 9 Mr. Enoch Powell, the Minister of Health, officially opened this clinic, which is an example of coordination between different parts of the National Health Service.

It is housed in premises, leased from the borough council, in Wandsworth municipal buildings. The day-to-day administration is in the hands of the Battersea and Putney Group hospital management committee, medical staffing is the responsibility of the board of governors of the Hospitals for Diseases of the Chest, and the London County Council provides almoner and health-visitor services. The Institute of Diseases of the Chest uses the clinic for postgraduate instruction. A coordinating committee, with representatives of these bodies and of the Wandsworth tuberculosis care committee, deals with any problems arising in the running of the clinic. The chest physician is Dr. K. M. Citron.

Identification Cards for Patients Receiving Steroids

The Minister of Health's Standing Medical Advisory Committee and the Central Health Services Council have approved a standard form of identification card to be carried by patients receiving steroid therapy. This is being supplied to hospitals through regional hospital boards, and to general practitioners through executive councils.

The card provides spaces for the name and address of the patient, and of his general practitioner, the name of the hospital he is attending and of the consultant or specialist who may be treating him, and details of drugs and dosages. It gives general instructions for the patient or anyone who finds the card in his possession. The size of the card is $5^1/_2$ in. by 4 in. and it fits, folded in two, into a transparent plastic envelope. It is intended for issue to all patients whose health might suffer if treatment were interrupted. It is essential that cards should be kept up to date and that they should be replaced as soon as they begin to become illegible through wear or other causes. It is suggested that patients should be informed of the purpose of the card, instructed to carry it at all times, and asked to produce it whenever treated. Some hospitals already issue cards, but it is desirable that these should be replaced by the standard card as soon as possible.

The inaugural meeting of the London group of the Anglo-American Medical Society will be held on Thursday, May 25, at 8.30 P.M., at the English-Speaking Union, Charles Street, Berkeley Square, W.1. The Oxford group will meet on Friday, May 26, at 4.30 P.M., at the U.S.A.F. Hospital, Burderop, near Swindon, when Dr. David Gold will speak on the treatment of mass casualties.

A meeting of the Biochemical Society will be held on Thursday and Friday, May 25 and 26, at University College and Trinity College, Dublin. This meeting will be followed by a meeting of the Association of Clinical Biochemists on Saturday, May 27, at 10 A.M., at University College, when the programme will begin with a symposium on acid-base balance.

A meeting of the Society for the Study of Infectious Disease will be held on Saturday, May 27, at 11 A.M., at Ruchill Hospital, Glasgow.

On Tuesday, June 6, at 8.30 P.M., at a meeting of the Anglo-Continental Medical Society at Manson Hall, Portland Place, London, W.1, Dr. Conrad Gasser of the University of Zurich will give a lecture on the leukæmias.

CORRIGENDA: "*Postcardiotomy Syndrome.*"—In this article by D. W. G. Smith (April 8, p. 750), the third paragraph should have opened: "The following case is reported because anticoagulant treatment, given for calf-vein thrombosis, was . . ."

The Premature Infant.—In this annotation (May 6, p. 985) the last sentence of the second paragraph should have opened as follows: "Apparently the commonest lesions in the infant leading to perinatal death are disorders of the respiratory system. . . ."

Diary of the Week

MAY 21 TO 27

Tuesday, 23rd

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Prof. E. I. Grin: Endemic Treponematoses.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. (Wright-Fleming Institute). Dr. R. M. Calman: Puerperal Infection.

Wednesday, 24th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
2 P.M. Dr. Kevin McCarthy: Recent Work with Measles Virus.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. W. Riddell: Virulence of Pathogenic Fungi.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. N. C. Oswald: Fatal Pneumonia.
EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Prof. C. D. Darlington: Cousin Marriage.

Thursday, 25th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. J. F. Goodwin: Cardiomyopathy.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. R. M. Harman: Further Benign Conditions Treated by Radiation.
IMPERIAL CANCER RESEARCH FUND
5 P.M. (Royal College of Surgeons of England, Lincoln's Inn Fields, W.C.2.) Mr. Denis Burkitt: Lymphoma Syndrome in African Children.
UNIVERSITY OF LEEDS
3 P.M. (Riley Smith Hall.) Sir Harry Platt: Moynihan—the Education and Training of the Surgeon. (Moynihan lecture.)
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. A. S. Relman: Acid Balance in Health and Disease.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Queen's College, Dundee.) Mr. A. P. M. Forrest: Pituitary Destruction and its Effects.

Friday, 26th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Mr. J. G. Murray: Advances in our Knowledge of Gastric Physiology.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Pædiatrics.* Prof. M. L. Rosenheim, Dr. John Hodson, Dr. David Edwards, Mr. Innes Williams: Hypertension in Childhood.
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4.30 P.M. (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Mr. F. E. Stabler: Flying Squad.

Appointments

BALDASERA, JOSEPH, M.B. Durh., F.F.A. R.C.S.: consultant anæsthetist, Sunderland hospital group.
BUSHELL, B. W. M., M.B. Birm., F.R.C.S., D.L.O.: part-time consultant E.N.T. surgeon, St. Antony's Hospital, Cheam, Surrey.
EADIE, J. W., M.B. St. And., F.R.C.S., F.R.C.S.E.: consultant general surgeon, Grimsby hospital group.
ISHERWOOD, IAN, M.B. Manc., F.F.R., D.M.R.D.: consultant radiologist, Derby hospital group.
MCDONALD, E. LAWSON, M.D. Cantab., F.R.C.P.: part-time assistant physician, National Heart Hospital, London.